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PATHOGENESIS OF ESSENTIAL HYPERTENSION*

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The purpose of this paper is to present in a preliminary way some suggestions in regard to the pathogenesis of essential hypertension. An introductory historical review of the subject is omitted, as several reviews are available already.

I. Evidence that Physiological Elevation of Blood Pressure Predisposes to Essential Hypertension in Later Life

Even when the blood pressures lie within limits regarded as normal, individuals whose pressures are higher than the average have a higher-than-average incidence of hypertension and circulatory disorder in later life, whereas those whose pressures are below the average have a decidedly lower-than-average incidence of essential hypertension and of circulatory disorders in later life (Symonds, 1923; Association of Life Insurance Medical Directors and the Actuarial Society of America, 1925; Diehl and Hesdorffer, 1933; Trans. Internat. Congress Life Ass. Med., 1935; Actuarial Society of America, 1939; Robinson and Brucer, 1939; Hunter, 1939; Hines, 1940; Actuarial Society of America, 1941).

Reference will now be made to some of the factors influencing the blood-pressure level. Especial attention will be given to the relationship of such factors to the expectation of the development of essential hypertension in later life.

Race and Geographical Environment

European and North American white people have somewhat higher average and modal casual blood pressures than certain Indian, Chinese, African, Philippine, and American Indian peoples, and the incidence of high blood pressure is decidedly lower among the latter group. The differences between the average blood pressures of such groups may be 10 to 20 mm. systolic and 8 to 15 mm. diastolic for comparable ages. While race seems to influence the liability to essential hypertension (Kirk, 1931; Shattuck, 1933; Flaxman, 1934; Kean, 1941) environment also has a strong influence; and this predisposition seems to be closely related to the levels of the blood pressures encountered in the populations under consideration.

For example, China appears to provide an environment favouring lower blood pressures and less essential hypertension. North America favours higher levels of the "normal" blood pressures and much essential hypertension. The blood pressure of Chinese in China is below that of Canadian and United States citizens resident in their own countries (Cadbury, 1922, 1923; Ying, 1926; Kilborn, 1926; Foster, 1927; Tung, 1928, 1930). Essential hypertension in much of China is also uncommon (Cadbury, 1922, 1923; Cruickshank, 1923; Kilborn, 1926; Foster, 1927, 1930) even among well-fed sections of the community (Houston, 1929). Krakower (1933–4) states that the blood pressure of Chinese after long residence in Canada resembles that of other Canadian residents, and that essential hypertension is common. Tung (1928) found that 30 Chinese resident in the United States had falls of pressure on returning to Peking. Tung (1927) reported that 58 Americans had a distinct fall of blood pressure on taking up residence in China, and Foster (1927) found that 120 Americans in Hunan had an average pressure close to that of the local Chinese.

African negroes have lower blood pressures than those of their race who live in America (Donnison, 1929), and the incidence of high blood pressure is low among negroes in Africa (Heimann, Strachan, and Heyman, 1929; Shattuck, 1930; Schulze and Schwab, 1936). The latter authors also quote personal communications from Taylor, Odaley, Dry, and Wakeford. American negroes after the age of 20 have higher blood pressures than American whites (Alvarez and Stanley, 1930; Adams, 1932), and the incidence of high blood pressure is greater in negroes than in white residents of the United States (Stone and Vanzant, 1927; Donnison, 1929; Alvarez and Stanley, 1930; Allen, 1931; Holmes, 1931; Kirk, 1931; Adams, 1932; Laws, 1932–3; Flaxman, 1934; Weiss and Prusmack, 1938; Hedley, 1941). Hypertension of a few days' duration after exposure to explosive blast was more common in negroes than whites (Ruskin, Beard, and Schaffer, 1948). Hypertension is greater among town dwellers than among country dwellers of the same race and land (Holmes, 1931; Flaxman, 1934). East Africans also have lower blood pressures and less essential hypertension than North American or Western Europeans (Donnison, 1929; Williams, 1944a, 1944b). Egyptians on the whole have lower blood pressures than Anglo-Saxon peoples and a somewhat lower incidence of essential hypertension (Ismail, 1928; Smirk, unpublished observations). British residents in Egypt have slightly lower blood pressures than the average in Great Britain (Smirk, unpublished observations).

The blood pressure in Filipinos and in Porto Ricans is lower than in people of the United States (Concepción and Bulatao, 1916; Ashford and Dowling, 1929; Torgerson, 1929; Salcedo and Pascual, 1932; Lantin, 1933), and hypertension is probably less frequent (Ashford and Dowling, 1929; Torgerson, 1929; Lantin, 1933).

Among the poorer classes in India blood pressures are lower (McCay, 1907) and essential hypertension is less common than in Anglo-Saxon lands (Raghavan, 1941).

The South American Indians of Yucatan have low blood pressures and a low incidence of essential hypertension (Shattuck, 1933). The Cuna Indians, living relatively isolated, had an average pressure of 105/69 for 407 adults, and no case of hypertension was discovered among them (Kean, 1944). The Zuni Indians have low blood pressures and little hypertension (Fleming, 1924).

Hicks (personal communication) found a systolic blood pressure of 110 was the most common in young Australian aboriginals, and in 120 aboriginals between 60 and 65 he found no blood pressures higher than 130 systolic. Benign hypertension is not uncommon in Australian Whites. Nye (1937) also remarks on the low incidence of hypertension in Australian aboriginals.

Certain environments favour higher "normal" blood pressures and other environments favour lower "normal" blood pressures. Populations exhibiting higher "normal" blood pressures have a higher incidence of essential hypertension and those with lower "normal" blood pressures have a lower incidence.

Heredity

Heredity influences the level of the blood pressure. According to Ayman (1936), the children of two hypertensive parents have higher blood pressures and a 47% chance of essential hypertension in later life. When both parents are normotensive the blood pressures of the children are lower and the chance of essential hypertension is only 3%. This evidence is well supported by observations on identical twins, though environmental differences may sometimes lead to different blood pressures in identical twins. Additional evidence is cited by Platt (1947).

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Obesity

Obesity is statistically associated with over-average blood-pressure levels (Dublin, Fisk, and Kopf, 1925; Huber, 1927; Hartman and Ghrist, 1929; Kirk, 1931; Nuzum and Elliot, 1931; Short and Johnson, 1939; Robinson, Brucer, and Mass, 1940; Adlersberg, Coler, and Laval, 1946). This relation is found not only in the common forms of obesity but also in the obesity of Cushing's syndrome and in cortical hyperadrenia. Under-average body weight is associated with under-average levels of the blood pressure (Symonds, 1923; Huber, 1927; Robinson, Brucer, and Mass, 1940). Over-average blood pressures in children of over-average weight is also reported (Stocks and Karn, 1924; Short and Johnson, 1939). Manifest essential hypertension is also more frequent in the obese (Symonds, 1923; Terry, 1923; Dublin, Fisk, and Kopf, 1925; Barach, 1928; Master and Oppenheimer, 1929; Gager, 1930; Kirk, 1931; Nuzum and Elliot, 1931; Palmer, 1931; Short and Johnson, 1939; Robinson, Brucer, and Mass, 1940; Rony, 1940; Moschcowitz, 1945; Adlersberg, Coler, and Laval, 1946). Essential hypertension and obesity are to some extent genetically determined (Gates, 1946), although the relationship between them is scarcely understood (O'Hare, Walker, and Vickers, 1924; Page and Corcoran, 1945). Like twins exhibit very similar body weights (Rony, 1940), and their blood pressure is usually about the same level (Weitz, 1923; Hines, 1937–8; Klemola, 1938).

The relationship of obesity to hypertension, however, is not purely genetic, for loss and gain of weight from altered food intake are associated with fall and rise of blood pressure. This relationship between alteration in body weight and blood pressure has been observed in the obese and in persons of normal weight, in normotensives (Benedict, 1915; Benedict, Miles, Roth, and Smith, 1919; Preble, 1923; Bauman, 1928; Master and Oppenheimer, 1929; Moschcowitz, 1945), and in hypertensives (Preble, 1923; Rose, 1923; Terry, 1923; Master and Oppenheimer, 1929; Moller, 1931; Moschcowitz, 1945; Adlersberg, Coler, and Laval, 1946). In normal dogs and in hypertensive (Goldblatt, 1947) dogs, Wood and Cash (1939) showed that gains and losses of weight were associated with rises and falls of blood pressure. The effect of overweight on the blood pressure in man seems to be more pronounced after 40, corresponding to the age when the incidence of essential hypertension rises.

The blood-pressure fall corresponding to an average reduction of 24 lb. (10.4 kg.) was about 32 mm. systolic and 16 mm. diastolic in the 72% of obese hypertensives in the series of Adlersberg, Coler, and Laval (1946), who had a fall of blood pressure. The difference in the average blood pressure between more or less unselected groups of overweight and underweight individuals is about 10 mm. systolic and 8 mm. diastolic. The effect of obesity is more obvious, however, when the comparison is made between the percentage of hypertensives encountered in individuals who are over the normal standard weight as compared with the percentage among subjects who are under the normal standard weight.

It is clear that overweight is associated with a tendency to higher blood-pressure levels, and in the course of time a higher incidence of essential hypertension. Under-average weight is associated with lower blood pressures and decreased tendency to essential hypertension in later life. Errors in blood-pressure measurement by cuff methods and due to upper-arm obesity require further evaluation.

Transient Blood Pressure Increases

Of the blood pressure rises which occur in response to emotion most are transient, but many are of longer duration (von Monakow, 1920; Fahrenkamp, 1926; Weitz and Sieben, 1926; Grollman, 1929; Houston, 1929; Brown, 1929–30; Alkan, 1930; Mueller and Brown, 1930; Stieglitz, 1930; Kronfeld, 1932; Schultz, 1932; Ayman and Goldshine, 1940; Alam and Smirk, 1943a, 1943b; Ehrström, 1945). Emotional rises of pressure of 10 or 20 mm. are common, and rises of 50 mm. or more are encountered.

Such transient pressure increases are exhibited particularly on the first visit in connexion with an examination for military service, life assurance, student health survey, or clinical examination. That most of these transient rises are due to emotion, tenseness, alertness, or some such mental state is very highly probable, because nearly all subside, sometimes in a few minutes, if the subject can be put at ease (Weitz and Sieben, 1926; Mueller and Brown, 1930; Ayman and Pratt, 1931; Alam and Smirk, 1943a, 1943b; Smirk, 1944, 1947; Kilpatrick, 1948). The pressure often can be made to rise promptly again if emotion be provoked, for example, by a tactless remark or the entry of a nurse with a tray of instruments (Alam and Smirk, 1943a; Kilpatrick, 1948). Those who exhibit such transient blood-pressure elevations have a much greater chance of developing permanent arterial hypertension later (von Monakow, 1920; Frost, 1926; Palmer, 1930; Stieglitz, 1930; Robinson and Brucer, 1939; Hines, 1940). Even in young people transient rises carry an enhanced expectation of developing essential hypertension later (Palmer, 1930; Diehl and Hesdorffer, 1933; MacKenzie and Shepherd, 1937; Master, 1943; Rogers and Palmer, 1944; Levy, White, Stroud, and Hillman, 1945a, 1945b).

I am aware of no evidence which points to the existence of any pathological process in young subjects exhibiting transient hypertension and which might explain it. Transient blood-pressure elevations in otherwise healthy individuals under the age of 25 probably represent physiological responses of a magnitude greater than average. These might occur if vasomotor reactions or the mental reactions to physical stimuli or stress are excessive.

The reactions to vasomotor reflexes, such as the cold pressor test of Hines and Brown (1935), and the blood-pressure-raising reflex from voluntary muscle (Alam and Smirk, 1937) are usually greater in cases of essential hypertension than in healthy subjects of the same age group (Alam and Smirk, 1938). The elevations of blood pressure in response to psychical stimuli and in response to cold do not invariably show parallelism (Ruskin, Beard, and Schaffer, 1948). Hines and Brown (1935) state that the pressure-rises in response to cold are greater in the children of hypertensive parents than in those of normotensive parents. They consider that hyper-reacting normotensives are more likely to develop hypertension in later life. Evidence in the same direction comes from Dieckmann and Michel (1935). Evidence against the views of Hines and Brown has been published (Pickering and Kissin, 1936; Yates and Wood, 1936; Feldt and Wenstrand, 1942; Russek, 1943; Russek and Zohman, 1945). The matter is not yet settled.

Not all patients respond to nervousness or tenseness by blood-pressure rises (Hall, 1927), but those who do, and whose environment causes nervous tension, may be expected to exhibit those increases more often than normal individuals. Fischer (1930) states that mental exertion unaccompanied by emotion had no notable effect on the blood pressure, whereas Hill (1898), Bickel (1914), and Gillespie (1924) report that mental work elevates the blood pressure. Changes in the mental state of melancholic and other psychotic and psychoneurotic patients may be associated with considerable alterations in the blood pressure (Mueller, 1922). There are large individual differences in the reactions to mental stimuli, but many authors consider essential hypertensives are over-reactive, overtense physiological types (Moschcowitz, 1919; Ayman, 1933; Menninger, 1938; Binger, 1945).

No doubt transient hypertension is due in many cases to a combination of vascular lability with emotional lability, but sometimes one or other of these will predominate. The more restless and competitive environment of urban as distinct from rural life has been held responsible in American negroes and whites for the higher incidence of essential hypertension in urban communities (Holmes, 1931; Hashimoto, Akatsuka, Tsujii, and Shiraishi, 1933–4; Schulze and Schwab, 1936). Stocks and Karn (1924) state that the average blood pressure of children is higher in schools with strict discipline than in those where discipline is lax. Tigerstedt (1926) refers to the higher blood pressures in students in the few weeks before an examination. Ruskin, Beard, and Schaffer (1948) report considerable hypertension of some days' duration in persons exposed to explosive blast. Fraser and Cowell (1918) refer to the higher level of the blood pressure in front-line troops

when compared with supporting troops, and somewhat similar results have been reported by others (Gelshtein, 1943; Ehrström, 1945; and Graham, 1945). It has been claimed by Farris, Yeakel, and Medoff (1945) that repeated exposure of rats to an air blast may set up a lasting arterial hypertension. This has been confirmed by Restall and Smirk (unpublished observations), who have shown also that this hypertension is not abolished by anaesthesia.

The tendency to exhibit transient hypertension in response to mental and other stimuli may be taken to indicate a physiological make-up which is likely to express itself in daily life by abnormally strong and frequent blood-pressure elevations. The balance of evidence suggests that such elevations, if sufficiently frequent or prolonged, predispose the subjects towards the development later of essential hypertension.

2. Casual, Basal, and Supplemental Pressures

If the level of the blood pressure in health is an important indication of the future liability to essential hypertension, it will be important to know what significance should be attached to single or to multiple readings of the blood pressure.

The blood-pressure level in a ward or consulting-room is not an accurate guide to the average blood pressure of the patient throughout the day and during the night (Brooks and Carroll, 1912; Müller, 1921; MacWilliam, 1923; Campbell and Blankenhorn, 1925–6; Friedlander, 1927; Ayman, 1931; Master, 1943; Gubner, Silverstone, and Ungerleider, 1946). Were it possible to obtain some indication of the average of the pressures to which the vascular system was exposed a much closer correlation between this average pressure and the subsequent development of essential hypertension might be possible. It is, however, possible to discover the ranges over which the blood pressure is likely to fluctuate.

The blood pressure, even in health, is not to be regarded as an indivisible unity but as having two components. If the blood pressure (systolic and diastolic) taken under ordinary clinical conditions be considered as the casual blood pressure and that taken under defined basal conditions as the basal blood pressure, the difference between the casual and the basal blood pressure may be described as the supplemental pressure (Alam and Smirk, 1943a; Smirk, 1944). The supplemental blood pressure is, by definition, that part of the casual blood pressure which represents the response to the person's physical, metabolic, and cerebral activity at the time of measuring the pressure. Kilpatrick (1948) has confirmed and extended my observations on the basal blood pressure and has shown that in health the basal blood pressure is a physiological constant for the individual. In a series of 50 normal subjects (Smirk, 1944) the basal and supplemental pressures were independent variables in the sense that the possession by an individual of a high basal pressure neither increased nor appreciably diminished the expectation of that individual having a high supplemental pressure. Analysis of further experiments by Kilpatrick gives the same result. In a sense, therefore, among normals a person comes into the higher pressure range through the statistical coincidence of having both a high basal and a high supplemental pressure.

During undisturbed dreamless sleep the supplemental pressure falls to, or almost to, zero, whereas the basal pressure is substantially unaffected. The cardiovascular strain will be less if a given level of the casual blood pressure is derived from a low basal pressure and high supplemental pressure than if the reverse holds. Clinical experience (Alstad and Smirk, unpublished) suggests that high casual blood pressures due chiefly to a higher basal pressure are of more serious significance than casual blood pressures of equal height caused chiefly by an increase in the supplemental pressure, but the latter may be associated with pathological sequelae of hypertension.

Further relevant observations on basal and supplemental pressures have been reported elsewhere (Alam and Smirk, 1943a, 1943b; Smirk, 1944, 1947; Kilpatrick, 1948). Statements are made that blood pressures over 135 in young adults are to be regarded as abnormal. It is suggested that the decision rests to some extent on our concept of abnormal. I believe some confusion would be avoided if the decision about the normality or abnormality of a blood-pressure level were held to depend upon whether it is attained through the normal operation of physiological processes or whether it is elevated to some extent by pathological processes. Moderate elevations of the blood pressure may at first be induced entirely by the operation of physiological processes. Some of these physiological processes are intrinsic and represent a physiological set or a resultant of the many intrinsic factors influencing blood pressure. Some factors influencing the blood pressure, such as geographical and social environment, are extrinsic, and others, such as obesity, are probably both intrinsic and extrinsic.

The hypothesis suggested by the circumstantial evidence outlined above is that physiological elevations of the blood pressure, if high enough or of sufficient duration, predispose strongly to, or in some cases cause, the development of a pathological elevation of the blood pressure—namely, essential hypertension. Those influences which lead to elevation of the basal pressure probably predispose more strongly to the subsequent development of essential hypertension than influences which elevate only the supplemental pressure.

3. Evidence that in Essential Hypertension Blood-pressure Elevation Sometimes Precedes the Development of Arteriolosclerosis

The evidence comes partly from the many clinical reports of high-blood-pressure tendencies at an early age, when primary pathological changes in the vessels are unlikely (Glomset, 1931; Ayman, 1934; Hines, 1940; Kerley and Lorenze, 1942; Levy, Hillman, Stroud, and White, 1944; Graham, Hines, and Gage, 1945; Platt, 1948), and partly from histological and renal function studies. The temporary nature of the blood-pressure rises initially also suggests that an established humoral mechanism (e.g., Goldblatt) is not operating at this early stage.

Cases of essential hypertension in which the kidney taken at necropsy was normal have been reported by many authors (Pal, 1919; Bell and Clawson, 1928; Moritz and Oldt, 1937; Fishberg, 1939; Garreton-Silva, Rodríguez, and Aspillaga, 1941), although most of them regarded this as an exceptional finding. When, however, cases are selected deliberately from patients in the early stages of the disorder, normal kidneys or those showing minimal changes are often encountered (von Monakow, 1920; Wallgren, 1922). Thus kidney samples from early cases, removed at biopsy in the course of sympathectomy operations by Castleman and Smithwick (1943), have shown few of the findings characteristic of the more advanced cases encountered at necropsy.

Scott (1944) and Goldblatt (1947) criticized Smithwick (1944), in that his biopsy samples were too small. Smithwick's histological observations, however, are supported by the finding of almost normal diodrast excretion, which corresponds with results published by Page and Corcoran (1945). My histological observations on post-mortem material from moderate hypertensives under the age of 40, and dying of unrelated disorders, suggest that recognizable defects in arterioles may be lacking. Where

arteriolar changes were found they were much less in degree than those exhibited by the arterioles of elderly normotensives.

Cox and Dock (1941) perfused the kidneys of patients with essential hypertension and of controls and found the flow through the kidneys decreased with age, the decrease being but little greater with essential hypertension kidneys than with control kidneys from the same age group. Kimmelstiel (1933), perfusing kidneys, found little vascular obstruction in many early cases of benign hypertension, with equal or greater vascular obstruction in some elderly normotensives. McGeorge (1945) demonstrated a decrement in the renal function with increasing age, and pointed out that the renal function of young hypertensives was similar to that of young normotensives and both exhibited a better capacity to concentrate urea and chloride simultaneously (Smirk, 1933–4, 1934) than either old normotensives or old hypertensives. The decrease in renal function progresses more rapidly in cases of essential hypertension than in non-hypertensive controls. It seems very probable that the decrements in renal function with advancing years in normotensives and in essential hypertensives are due largely to decrease with age in the blood supply to the kidneys, with a more rapid decrease in the latter. Aitken in his unpublished work for a New Zealand M.D. thesis in 1944 undertook at my suggestion some observations on injected specimens of kidneys from young subjects of essential hypertension and also found the vascular beds to be substantially normal.

Indeed, it would seem that the evidence of gross pathology, microscopical pathology, intra-arterial injection studies of kidneys, biopsy studies of kidneys, perfusion of dead kidneys, renal function tests of various kinds, and the intermittent character of the blood-pressure increase in its early stages all suggest that the degree of permanent renal ischaemia in the early stages of essential hypertension *in young subjects* is unimportant and is not to be regarded as an adequate explanation of the blood pressure increases. *The evidence available at the present time suggests that when the disorder starts or when a "prehypertensive" state is present in comparatively young people the elevation of the blood pressure is often, probably usually, manifest before the characteristic pathological changes make their appearance in the kidney and in other organs.*

In many patients, however, the blood pressure does not start to rise appreciably until after the age of 40 or 50. When the blood pressure first rises after the age of 45 pathological changes in renal arterioles of one kind or another will almost certainly be present before the blood-pressure increase has reached the level ordinarily regarded as abnormal. It is possible, therefore, that in at least some of the cases in which the blood pressure begins to rise appreciably for the first time in middle life the renal ischaemia may have initiated the increase.

4. Evidence that High Blood Pressure Accelerates or Causes the Development of Arteriolosclerosis

In almost every muscular organ an increase in work beyond the physiological range of any kind of muscle—cardiac, voluntary, or involuntary—leads to hypertrophy. The cardiac hypertrophy in hypertension and the development of voluntary muscles with physical labour are well known. In the alimentary, urinary, and biliary tracts partial obstruction leads to hypertrophy of the muscle behind the obstruction. In the larger vessels of well-established cases of essential hypertension hypertrophy of the media is encountered. Vascular hypertrophy is seen in small pulmonary arteries obstructed by the bilharzia ova (Shaw and Ghareeb, 1938).

The walls of veins hypertrophy when exposed to raised pressure in arteriovenous aneurysm, the portal veins in cirrhosis of the liver, and the great systemic veins in congestive heart failure (Pei-Lin Li, 1940). In high blood pressure of varying types, essential hypertension, glomerulonephritis, pyelonephritis, polycystic kidneys, medullary hyperadrenia, cortical hyperadrenia, and in experimental hypertension of different types the typical thickening in the walls of arterioles has been described. Such changes may occur even in young children with hypertension of various origins. It seems that this hypertrophy also is due to the effect of increased pressure on the walls of blood vessels. Although the vast majority of observations strongly favour the idea that high blood pressure can cause hypertrophy of the walls of arterioles and of larger arteries a certain amount of evidence is either opposed to or fails to support this idea. In coarctation of the aorta it is stated (Graybiel, Allen, and White, 1935) that the arterioles in muscle samples taken in the upper part of the body showed no hypertrophy when compared with muscles taken from the lower part of the body. On the other hand, arteriolar hypertrophy in coarctation cases has been reported (Heyer and Keeton, 1941).

Again, there are a number of instances in the literature of high blood pressure of appreciable duration with few changes in the arterioles. In experimental hypertension in animals of various types arteriolar changes are sometimes found and sometimes lacking (Hamperl and Heller, 1934; Wilson and Pickering, 1937–8; Wilson and Byrom, 1939). Negative results may mean that there has not been enough time for hyperplasia or that the degree of increase in the blood pressure was insufficient. It seems that the dog often can tolerate prolonged experimental hypertension without exhibiting substantial arteriolar changes; on the other hand, it has been shown by Wilson and Byrom (1939), in the rat, that high blood pressure induced by ischaemia of one renal artery may lead to typical changes in the arterioles of the non-ischaemic kidney.

The observations of Wilson and Byrom were not accepted by Goldblatt and Kahn (1940), on the grounds that white rats are particularly susceptible to pyelonephritis, and the latter workers considered that the results obtained might have been explained by the development of this condition. Restall (unpublished observations) has shown that rats rendered hypertensive for a period of approximately one year by unilateral renal ischaemia exhibit arterial changes in the other kidney. His histological observations and the bacteriological studies by Kirschner rule out pyelonephritis in most of the experiments.

That high blood pressure gives rise to medial hypertrophy in the smaller arteries and in arterioles may be regarded as proved. There is also evidence that other arteriosclerotic changes, such as increase of elastic tissue and perhaps intimal hyperplasia (Restall, unpublished observations), may develop as the result of increased intravascular tension. The literature is summarized by Hueper (1944). The arteriolar changes secondary to high blood pressure are usually more pronounced in the kidneys than in other organs.

5. Ways in which Pathological Changes Induced or Accelerated by Hypertension may lead to Further Elevation of Blood Pressure

It seems probable that, irrespective of the cause, prolonged elevations of the blood pressure of sufficient degree both physiological and pathological, tend to be followed by processes which lead to the further elevation of the blood pressure, with the ultimate development of essential hypertension. Any pathological or physiological changes brought

about by the primary hypertension and leading to secondary rises of blood pressure could set up a vicious circle. At least five such mechanisms must be discussed.

(i) Inelasticity of Larger Arteries

In hypertension, arteriosclerosis of great vessels is accelerated with the loss of distensibility (Bramwell, 1924; Fahr, Davis, Kerkhof, Hallock, and Giere, 1932; Wiggers, 1938) causing systolic hypertension. It is stated that the mean blood pressure is not raised (Fahr, Davis, Kerkhof, Hallock, and Giere, 1932), and therefore it is uncertain whether such hypertension will or will not tend to accelerate arteriosclerosis and arteriolosclerosis further. *It is not suggested that this systolic hypertension caused by decreased elasticity of large arteries is sufficient to explain the progressive increase of blood pressure, but that it is a factor which participates.*

(ii) Exaggerated Contraction of Hypertrophied Arterioles

Measurements of arterioles and small arteries in almost all tissues of the body, and notably in muscle, indicate that at a certain stage in the development of essential hypertension there is medial hypertrophy. It seems likely that more vigorous responses by hypertrophied blood vessels would account for the fact that both rises and falls of blood pressure in response to various stimuli are commonly exaggerated in essential hypertension. Experimental evidence in favour of this has been obtained by Restall (unpublished observations), who compared the response to adrenaline of blood vessels from chronically hypertensive and control rats, and found greater responses from the vessels of hypertensives, especially renal vessels. Even if medial hypertrophy does not of itself raise the blood pressure it seems probable that it would render other hypertensive agents more effective. *If the medial hypertrophy caused by blood-pressure elevations leads to further increase of the blood pressure another vicious circle has been set up.*

(iii) The Goldblatt Mechanism and Variable Reactivity of Blood Vessels to Pressor Agents

The suggestion has been made that essential hypertension might be due to the liberation of pressor substances from kidneys rendered ischaemic by arteriolar changes in the renal blood vessels (Goldblatt, 1947). The arteriolar changes in essential hypertension are most prominent in the kidney (Fahr, 1922; Fishberg, 1925; Russell, 1929; Moritz and Oldt, 1937; and others). I favour the view that such arteriolar changes, more particularly in the later years, may occur primarily, but some at least of them may be caused or accelerated by the prodromal rises of blood pressure referred to in the first part of this paper.

The experimental evidence that ischaemic kidneys sometimes liberate pressor substances is so strong that it may be taken as proved. The presence of some degree of renal ischaemia in almost all advanced cases, especially elderly cases, may be regarded as established. It seems probable that such renal ischaemia will cause a rise in blood pressure at certain stages and in certain cases of established essential hypertension. The suggestion has been made also that functional renal vasoconstriction might initiate a Goldblatt type of hypertension (Goldring, Chasis, Ranges, and Smith, 1941). At my suggestion Restall (unpublished observations) studied the response to adrenaline of blood vessels in rats rendered chronically hypertensive by unilateral renal ischaemia and in control rats. He found that vasoconstriction was much more pronounced in the vessels of the unoperated kidneys of the hypertensives than in the renal vessels of controls. Such observations indicate a means by which renal vascular changes may become progressive.

On the other hand, renal ischaemia is not always associated with an elevation of the blood pressure (Kimmelstiel, 1933; Cox and Dock, 1941). Whether the absence of hypertension is due to failure of the kidneys to release pressor agents, to the subsequent inactivation of such agents (Fasciolo, Houssay, and Taquini, 1938; Katz, Mendlowitz, and Friedman, 1938; Rodbard and Katz, 1941), to the operation of homoeostatic controls preventing an elevation of the blood pressure, or even to antipressor agents, it is impossible to say at the present time. The experimental study of renal hypertension is made more difficult by the fact that the available experimental animals behave dissimilarly (Braun-Menéndez, Fasciolo, Leloir, Munoz, and Taquini, 1946). In the rat and rabbit it has been suggested that, whereas the initial rises of blood pressure following renal ischaemia are due to the Goldblatt mechanism, the subsequent maintenance of the high blood pressure is effected by some other means. The application of the results to human hypertension remains uncertain. The processes whereby renal ischaemia leads to hypertension in experimental animals is complicated and not yet fully evaluated. Liberation of an enzyme-like substance, renin, from the ischaemic kidney acts upon a substrate-like substance, preangiotonin, which is a constituent of plasma, to form a pressor agent, angiotonin. The angiotonin causes vasoconstriction by a direct action on smooth muscle, but has a limited period of action owing to its enzymic destruction.

From the observations of Black (unpublished) it seems that, apart from destruction, the amount of circulating angiotonin could not be the only factor deciding the magnitude of blood-pressure increase. Black has shown that there is no consistent difference between hypertensives and normotensives in respect of their sensitivity to the pressor action of intravenous angiotonin. Some individuals are insensitive to doses of angiotonin which in others cause large rises in blood pressure. Vascular sensitivity to the pressor action of angiotonin runs parallel with sensitivity to the pressor action of S. methyl isothiourea. A non-specific reactivity of blood vessels governs the pressor response as well as the amount of circulating angiotonin.

The formation of hypertensive agents depends upon the degree of ischaemia and the amount of renal tissue involved; and the rate of destruction of hypertensive agents is related to the amount of non-ischaemic renal tissue in the body. The kidneys both of essential hypertension and of elderly normotensive cases may have within them areas which are ischaemic and areas which are adequately supplied with blood. It is therefore possible that while parts of the renal tissue are forming, other parts may be destroying, the hypertensive agents. Increased formation of V.E.M. or decreased elimination of pressor amines by amine oxidase have been suggested as alternative or additional mechanisms by which renal ischaemia could cause blood-pressure elevations. *It seems clear, however, that elevated blood pressure favours renal arteriolosclerosis, and if this in turn gives rise sometimes to further elevations of the blood pressure due to the renal ischaemia a vicious circle would be set up.*

(iv) Elevations of the Blood Pressure Persisting After the Initial Cause has Ceased to Operate

(*a*) *Hypertension Persisting After Removal of a Single Ischaemic Kidney.*—In the rat the removal of the ischaemic kidney after several months of experimental hypertension did not usually restore the blood pressure to normal (Wilson and Byrom, 1941; Grollman, Harrison, and Williams, 1943; Patton, Page, and Ogden, 1943). It seems that in many cases pathological changes have developed in the unoperated kidney (Patton, Page, and Ogden, 1943; Restall, unpublished observations), and the persistence of the blood-pressure elevation has been attributed to these. Pickering (1945) has indicated the possibility of a non-renal mechanism. Likewise in the rabbit Grollman (1944) found that nephrectomy after ten weeks of hypertension from renal compression does not abolish the hypertension. In the dog the evidence is insufficient. It has been shown that removal of a single ischaemic kidney abolishes the hypertension in the dog if the removal is carried out within the first few weeks (Goldblatt, Lynch, Hanzal, and Summerville, 1934; Blalock and Levy, 1937; Houssay and Fasciolo, 1937; Verney and Vogt, 1938, 1943; Rodbard and Katz, 1939). Isolated experiments suggest that, in the dog, hypertension may persist if removal of the ischaemic kidney is postponed for three months or more. Goldblatt, however, reported an experiment in a dog with unilateral renal hypertension of nine months' duration which was completely cured by nephrectomy.

(*b*) *Hypertension Persisting After Bilateral Nephrectomy.*—Pickering (1945) has shown that blood-pressure elevations may be made to outlive the stimulus which produced them. He raised the blood pressure in rabbits by unilateral nephrectomy and constriction of the main artery of the remaining kidney, and noted that if hypertension had lasted but a few days and

the remaining ischaemic kidney was removed the blood pressure fell to normal in a few hours. If the hypertension had lasted seven weeks or more excision of the ischaemic kidney no longer removed the hypertension. The response of the blood vessels was altered as the result of the prolonged hypertension. There are clinical experiences which may be analogous. For example, where the blood-pressure rise due to toxaemia of pregnancy has been of short duration, even if high, termination of the pregnancy often is associated with a comparatively rapid fall of the blood pressure back towards normal. If, however, the blood-pressure rise has been of long duration the blood pressure may not return to normal for several months after the termination of the pregnancy, and in some cases a permanent hypertension results. The incomplete fall or absence of a fall of blood pressure following the removal of a unilateral ischaemic kidney even when there is good evidence that the remaining kidney is healthy (Abeshouse, 1941a, 1941b) may be another example.

Some observations concerning the effect of bilateral nephrectomy by Flemming (unpublished observations) on hypertensive rabbits confirm the observations of Pickering.

(*c*) *Experimental Audiogenic and Neurogenic Hypertension.*—Medoff and Bongiovanni (1945) and Farris, Yeakel, and Medoff (1945) showed that rats subjected for long periods to intense intermittent audiogenic stimuli developed elevations of blood pressure. Restall and Smirk (unpublished observations) confirmed these findings and found in agreement with Medoff and Bongiovanni that the blood-pressure elevations were not abolished by light or ether anaesthesia. We noted that the blood-pressure increase persisted for at least several months after the audiogenic stimulation ended, that there was no histological evidence of renal damage in the early stages of the experimental hypertension, and that the blood pressure remained elevated for 36 hours after bilateral nephrectomy. The possibility that the nervous system was damaged by supersonic waves has not yet been eliminated.

In some other experiments, however, rats were exposed first to a signal noise (buzzer), no question of supersonics being involved. The signal noise was followed by electrification of the cage causing a mild-to-moderate faradic stimulation of the rats' feet. This also led within a few weeks to a rise of blood pressure, though of smaller degree, which was not abolished by light ether anaesthesia. It seems that the initial blood-pressure elevation is due in this case to nervous stimulation, and that this has given rise to an increase in blood pressure which apparently is maintained by some process other than that which initiated the hypertension.

This would appear to be experimental confirmation in the rat of the suggestion that certain blood-pressure increases if frequent or prolonged enough may outlive the stimuli which caused them. These persisting blood-pressure increases in rats following audiogenic and electrical stimulation often persist after bilateral nephrectomy, and in this resemble those described by Pickering (1945) in rabbits after hypertension induced by renal ischaemia. Apart from the general resemblance there is as yet no evidence of a single underlying mechanism. The significance for human hypertension is undetermined.

(v) Absence of Appreciable Increase of Passive Resistance in Hypertrophied Vessels

The idea that pathological changes in the arterioles may result in a permanent increase in the peripheral resistance and thereby be responsible for continued elevation of the blood pressure was discussed by Volhard (1931). The elevation was looked on as being passive and anatomical rather than contractile in origin. The changes in the blood vessels outside the kidney, however, are thought to be insufficiently advanced to give support to this explanation. The considerable fall in blood pressure which may occur for a short time after sympathectomy, after nitrates, or from thiocyanate overdosage suggests that no great part of the peripheral resistance is the result of purely passive changes in the vascular bed. Restall perfused through the aorta the hind quarters of rats which had been hypertensive for a period of 12 to 18 months (approximately one-third to one-half of the normal duration of a rat's life), and, compared with normal rats, he found but little difference in the peripheral resistance. It appears from th experiment that the continued high blood pressure was ma tained by active vasoconstriction and even after one year on a minor part of the peripheral resistance of the lower lim was of a passive character. *I have not, therefore, been ab to find experimental support for the idea that pathologic changes in vessels lead in time to the development of a important generalized increase of passive peripheral resistan*

6. Other Factors which may Elevate the Blood Pressu

1. *Increased Reactivity to Blood-Pressure-Raising Reflex in Cases of Arterial Hypertension.*—High reactivity to th cold pressor test (Hines and Brown, 1935) and to the bloo pressure-raising reflex from muscle (Alam and Smirk, 193 is often encountered in essential hypertension, but th does not by itself explain a high level of the *resting* bloo pressure. It is probable that a high degree of reactivity the blood pressure to blood-pressure reflexes may expre itself in daily life by abnormally strong and frequent bloo pressure variations. The blood pressure from this cau may be found at a higher level in the non-basal condition which ordinarily are present at the time of measurement The reactivity to blood-pressure-raising reflexes increase with age, but to a greater degree in essential hypertensio than in health (Alam and Smirk, 1938 ; Russek and Zohman 1945).

2. *Natural Increase of Blood Pressure with Age.*—The recorded blood-pressure averages increase with age. To some extent this is due to the effect of including th pressures of hypertensive individuals in the figures. The general impression, however, is that there is also an increas in the average blood pressure with age which does no depend on the inclusion of hypertensives. This "natural" blood-pressure increase with age is likely to be one of the several factors responsible for the increase in the incidenc of essential hypertension in the later years of life.

3. *Alteration in the Response of the Carotid Sinus t Blood-Pressure Increase.*—While my observations confirm Pickering, Kissin, and Rothschild (1936) in their view tha the carotid sinus mechanism in cases of essential hyper tension responds to digital stimulation, I found that in response to blood-pressure increases produced reflexly the pulse rate tends to rise instead of falling in most cases o essential hypertension, the natural relationship betwee pulse rate and blood pressure being reversed (Alam an Smirk, 1938). A corresponding observation was mad previously by MacWilliam (1925). A possible interpreta tion of this is that the carotid sinus offers a less effectiv control over the blood-pressure level in cases of essentia hypertension.

4. *Increase of the Secretions of the Suprarenal Gland.*—The suggestion has been made that cortical hyperadrenia may be concerned in the pathogenesis of essential hyper tension (Perera, Knowlton, Lowell, and Loeb, 1944 ; Perera and Blood, 1947a, 1947b). In terms of the present hypothesis, blood-pressure increases of suprarenal origin or any other, if sufficiently frequent and prolonged, would be expected to play their part in pathogenesis.

Comment

If elevation of the blood pressure in essential hypertension depends upon the total effect produced by the combined action of several components, it becomes important to know whether the magnitude of the total effect is equal to the sum of the effects of the various components acting separately. The answer appears to be that the blood-pressure rise produced by two blood-pressure-raising stimuli acting simultaneously is less than the sum of the blood-pressure rises produced by the two stimuli acting separately (Bruce, Martin, and Smirk, 1945). This may be a part of the

explanation of why the rate of increase of the blood pressure is slowed up as higher levels are attained.

No reference has been made earlier in this paper to malignant hypertension, largely because it is thought that malignant hypertension is something other than a severe or accelerated form of essential or benign hypertension. After a survey of 169 consecutive deaths in hypertensive individuals, residents of the province of Otago, New Zealand, and on the basis of clinical experience in that province, Alstad and Smirk (1948) reached the conclusion that, whereas benign hypertension is a very common condition, malignant hypertension and the classical advanced glomerulonephritis are both most exceptional, particularly the former. It is sometimes stated that malignant hypertension is an accelerated form of benign hypertension. But experience goes to show that benign hypertension in Otago province does not differ fundamentally from benign hypertension in other countries, although its course appears to be rather milder; yet malignant hypertension is decidedly uncommon. It seems very probable, therefore, that the condition of malignant hypertension is not merely an accelerated form of benign hypertension but involves some additional factor over and above those responsible for benign hypertension. It is of great interest that there is also a correspondingly low incidence of chronic glomerulonephritis in Otago province. It is clearly worth considering whether the infrequency of advanced chronic glomerulonephritis and of malignant hypertension in this province is in some way related to the absence of a common aetiological factor.

Summary

It seems probable that there is no single or simple primary cause of essential hypertension.

It is thought that the disorder may originate in some cases from the simple overactivity of physiological processes, whereas in other cases pathological changes such as renal arteriolosclerosis may be primary.

It is suggested that the blood-pressure increases are of composite origin but that these increases, if frequent, high, or prolonged enough, give rise to a number of pathological and functional changes which tend to maintain or elevate the blood pressure further. Once this self-perpetuating cycle of changes has been set up the condition may be described as essential hypertension. Under-average blood pressures are associated with a much decreased incidence of essential hypertension in later life. It is difficult to explain this protective influence of low blood pressure except by the hypothesis that the tendency to develop high blood pressure in later life is influenced strongly by the precise level of the blood pressure even when this lies within the normal range.

Examples of factors various combinations of which may raise the level of the blood pressure enough to enhance strongly the liability to the subsequent development of essential hypertension include: certain geographical environments, race, heredity, emotional lability or disposition to over-alertness and tenseness, occupations or domestic environments involving a tendency to stress and strain, over-average liability of the vasomotor system to respond by vasoconstriction to tenseness and emotion, physical activity or metabolic stimuli, over-average body weight or sthenic habitus.

Elevations of the basal pressure are likely to throw greater strain on the heart and on small arteries and arterioles than are elevations of the supplemental pressure.

The degree to which blood vessels are able to withstand exposure to over-average blood pressure or vasoconstriction without undergoing pathological change varies from one individual to another and is likely to have an important influence both on the rate of increase of the blood pressure and on the development of complications.

Examples of a number of pathological and functional changes which in various combinations it is thought might be responsible for further elevations of the blood pressure are cited and discussed in the text. These include: (*a*) inelasticity of large arteries; (*b*) exaggerated contraction of hypertrophied arterioles; (*c*) the release of pressor agents from ischaemic kidneys; (*d*) to a very minor degree, increased passive resistance of hypertrophied arterioles; and (*e*) an unknown non-renal factor or factors capable of perpetuating certain blood-pressure increases after the primary exciting causes of these increases have ceased to operate. Other factors are referred to which probably contribute increments of pressure increase.

The fundamental unity of the clinical picture in essential hypertension is not dependent upon the blood-pressure elevation being regarded as the result of a single or simple pathological process. It is due to the fact that the clinical manifestations and complications are due almost entirely to events which are secondary to a single characteristic of the disorder —namely, high blood pressure brought about mainly by vasoconstriction.

The above general hypothesis holds that elevations of blood pressure in man and certain other mammals tend to be self-perpetuating. It is to be expected, therefore, that the cycles of changes concerned in the secondary elevations of the blood pressure which occur in essential hypertension will be responsible *in part* for the perpetuation, and perhaps for the further increase, of blood pressure in certain other conditions such as post-toxaemia of pregnancy, cortical hyperadrenia, and some cases of chronic pyelonephritis, medullary hyperadrenia, and chronic nephritis.

There is evidence suggesting that malignant hypertension is something other than an accelerated form of benign or essential hypertension.

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THE ROLE OF INFECTION IN GRANULOPENIA

BY

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In 1922 Schultz first reported a condition of severe and progressive oral sepsis associated with granulopenia, which often ended fatally. There can be no doubt that in the earlier cases the importance of sepsis was realized and stressed, but during the twenty years which followed Schultz's paper the aetiological emphasis shifted from infection to the leucotoxic drugs, the administration of which often coincided with the appearance of "malignant neutropenia," as this syndrome was now called.

Reports of cases associated with the taking of compounds containing amidopyrine began to appear on the Continent in 1930, and later in this country. The evidence against these drugs seemed irrefutable, particularly when it was shown that, in some patients who had recovered, a further small dose immediately produced a profound fall in the number of circulating granulocytes. With further experience other therapeutic agents fell under suspicion, and cases of dangerous neutropenia were reported after the use of organic arsenic, gold salts, sulphonamides, and, more recently, the thiouracils. This list is by no means complete, but is sufficient for the present purpose.

As familiarity with the condition increased, more and more importance was focused upon the leucotoxic agent, while the infection which invariably accompanied the condition came to be regarded as a purely secondary matter, due to invasion of the defenceless organism by bacteria. Thus Wilkinson (1936) uses such phrases as "the primary cause is clearly not bacteriological" and "it is apparently true, however, that the oral, throat, and other ulcerative or necrotic lesions are secondary to the blood condition, and not vice versa."

This view has undoubtedly held the field with little or no question, though all writers on the subject have referred to the fact that malignant neutropenia is from time to time encountered in certain severe infections, particularly staphylococcal septicaemia and osteomyelitis, pneumonia, and liver abscess, when none of the usually accepted leucotoxic drugs have been used. Witts (1936) points out that patients whose white cells have been depressed by one of these drugs may or may not develop the acute illness, depending upon chance exposure to infection. He also refers to animal experiments which seemed to show that such drugs make impossible the normal leucocyte response to infection.

Dameshek and Wolfson (1942) made a preliminary report on the treatment of agranulocytosis by sulphonamides. Nixon, Eckert, and Holmes (1943) described three cases in which agranulocytosis developed while infections were being attacked by sulphadiazine. Instead of withdrawing the drug, it was continued in larger doses, with the result that the blood pictures returned to normal and the patients recovered.

Since these papers, the part played by infection in granulopenic conditions has assumed increasing importance. There can be no doubt that many physicians have accepted Dameshek's advice regarding treatment and no longer worry about the blood picture, concentrating their efforts in overcoming the infection which is threatening to overwhelm the victim.

Boland, Headley, and Hench (1946) reported the cure of a case of total agranulocytosis following the use of gold—a particularly fatal combination—by means of penicillin. In the same paper they refer to fourteen other cases associated with various drugs successfully treated in the same way.

Nevertheless, Israëls (1948), writing of penicillin treatment, says: "Several cases have been reported in the literature, but the results are not very convincing. If there is evidence of sepsis, it is clear that penicillin should be given promptly." Acute agranulocytosis unassociated with sepsis must be exceedingly rare, though Hickie (1948) has described the case of a 70-year-old man whose blood appears to have been almost devoid of cells of the granular series for a period of three years, and in whom it seems that sepsis was infrequently seen, and only as mild superficial episodes.

In March, 1946, I had under my care a woman who developed a complete agranulocytosis while undergoing treatment with gold for rheumatoid arthritis. Two previous similar cases under my care had quickly ended fatally in spite of vigorous treatment, using all the recognized methods of bone-marrow stimulation. In this case penicillin was added to the treatment, and recovery was prompt and complete.

A Series of Cases

While serving on the Medical Division of a military hospital during 1947 I had the opportunity of treating a number of cases in which severe granulopenia complicated arsenical treatment of syphilis. In addition to N.A.B. all these cases were receiving bismuth, an agent which appears in the list of leucotoxic materials given by Beaumont and Dodds (1947), though I have been unable to discover the report of any case in which granulopenia followed the use of bismuth without arsenic.

In the earlier cases British anti-Lewisite (BAL), "pentide," blood transfusion, ascorbic acid, liver extract, and other bone-marrow stimulants were used in addition to penicillin. In six subsequent cases penicillin alone was employed, with very satisfactory results. McManus (1946) records a similar experience. A case of "arsenical agranulocytosis" treated with BAL and pentide failed to improve until penicillin was added to the treatment. In a second case cure was rapidly achieved by the use of penicillin alone.

In every instance sepsis, particularly in the mouth, was striking and severe, and haematological improvement went hand in hand with resolution of the infection. This was so striking that I wondered if the infection was of greater importance in the causation of the condition than the arsenic. I wondered, too, if it could be shown that cure could be assured, provided the infection was controlled, even when further arsenic was administered. Further cases of arsenical granulopenia provided the material necessary to put this view to the test.

Several doses of N.A.B. were given to a man (Case 1) immediately after his recovery from the acute illness, for which he had been treated with penicillin alone. These produced no untoward effects either clinically or in the blood picture, and he went on to complete his full course of antisyphilitic treatment. In Case 2 the same procedure was followed, with the same result.

It now remained to observe the effect of arsenic administered before the acute illness had been controlled. In Case 3, 0.6 g. of N.A.B. was given 24 hours after starting penicillin. This appeared to make no difference to the patient's response to treatment. In Case 4 a full dose of N.A.B. was given before starting penicillin treatment. In this case recovery was somewhat delayed, but it was discovered that the infection involved a penicillin-resistant strain of staphylococcus, and the local sepsis did not respond until very large doses of the antibiotic had been given. The haematological improvement followed immediately upon control of the local infection. Reports of the four cases are given below.

Case 1

A private soldier aged 25 was admitted seven weeks after starting routine treatment for a dark-ground-positive chancre. Treatment had been interrupted by mild febrile reactions to arsenic injections, and on admission he had received 3.15 g. of N.A.B. and 1.4 g. of bismuth in addition to 4 mega units of penicillin.

He presented with gross oral sepsis, the gums, which were swollen and congested, being particularly affected. His temperature was 104° F. (40° C.) and his pulse rate 110. There was considerable adenopathy involving all the superficial glands, his spleen was palpable, and he was covered with a well-marked pigmented secondary syphilide. His white cells numbered 5,000 per c.mm., only 5% of which were of the granular series (total polymorphs 250). The Kahn test was positive, two units, and the Paul–Bunnell test negative. He was treated with 50,000 units of penicillin three-hourly. At the end of 48 hours, with his temperature falling and his mouth improving, his white cells numbered 6,000, 24% of which were granulocytes (total 1,440). On the fifth day his temperature was normal, and his mouth almost normal, while his white count had risen to 7,600, 43% polymorphs (total 3,268). Two days later, the penicillin being continued, 0.3 g. of N.A.B. was injected intravenously. There was a slight febrile reaction, but his white cell count remained satisfactory; indeed, when comparing counts made immediately before the injection with those made at 12 and 18 hours after the injection there was a definite increase in the number of circulating polymorphs.

Two days later a further injection of 0.45 g. of N.A.B. was given. To this injection there was no reaction, but 36 hours later he showed a leucocytosis of 20,000 with 65% polymorphs (total 13,000). During this stage of treatment penicillin cover had been maintained. This was now discontinued, and he subsequently completed his course of antisyphilitic treatment with N.A.B. and bismuth without further incident, his blood count remaining normal throughout.

Case 2

A soldier aged 24 should have received his final dose of N.A.B. and bismuth on July 5. This was withheld because of swollen gums, and he was referred to the dental department. He was admitted three days later with a temperature of 104° F. (40° C.), pulse 130, and showing gross swelling of his lowe jaw, gingivitis, and many boils on the arms and trunk. He ha received 7.5 g. of N.A.B. and 2.6 g. of bismuth. His bloo showed 3,650 white cells per c.mm., with 10% polymorphs (tota 365). The Kahn test was negative. Penicillin was started 50,000 units being given every three hours. His response wa immediate, and in 24 hours his temperature had fallen t 100° F. (37.8° C.) and there was considerable local improve ment, while his polymorph count had risen to 896. Three day later the condition of his mandible and gums seemed normal while all his boils had healed and his white cell count showe that 56% of 3,600 cells were polymorphs (total 2,016). Penicil lin was discontinued, and two days later, with a normal whit cell count, he was given 0.45 g. of N.A.B. intravenously. Thirty six hours after the injection he showed a leucocytosis of 14,00 with 64% polymorphs (total 8,960). Two weeks later his whit cell count was normal.

Case 3

A 43-year-old officer received his fifth injection of arseni on Oct. 16. The total amount of arsenic received was 2.55 On the 18th his mouth and gums became painful. He wa admitted on Oct. 25 with high fever, great swelling of the gums and buccal ulceration. His white cell count was 6,200 per c.mm. with 18% polymorphs (total 1,116). Treatment was withheld and the next day his count had fallen to 5,100, with 16% polymorphs (total 816). Penicillin was now started—50,00 units three-hourly—and by the 27th, with clear-cut clinical improvement, his white cells had increased to 6,000, 32% o which were polymorphs, 9% being eosinophils (total granulo cytes 2,460). N.A.B. 0.6 g. was given intravenously on thi day. An urticarial rash resulted, lasting 24 hours. Next day with his temperature normal and showing marked local improvement, his white cell count had improved to 7,100 (52% polymorphs, 7% eosinophils; total granulocytes 4,189). From this point his illness rapidly resolved, and he was discharge to continue his course of antisyphilitic treatment, without further episode.

Case 4

A private soldier aged 20 was admitted on Dec. 3. H had received 1.95 g. of N.A.B. and 0.8 g. of bismuth. Th earlier stages of his arsenical treatment had been decelerate on account of some skin reactions. Two days before admissio he had felt ill, with pain in his left cheek. The next day th cheek was swollen and a sty had developed on the right lowe lid. He reported sick and was sent to hospital 24 hours late He then had a temperature of 104° F. (40° C.) and showe all the signs of considerable toxaemia. On the buccal surfac of the left cheek there was a deep painful ulcer. The le lower lid had a staphylococcal infection, and furuncle wa present on his chin. A blood count showed 4,200 white cel per c.mm., 2% of which were polymorphs (total 84). Before th beginning of treatment he was given 0.6 g. of N.A.B. Two hour later penicillin was started in 100,000-unit doses every thre hours. The next day his white count had fallen to 2,400 an no polymorphs could be seen in a smear. Subsequent coun were as follows:

Date	Leucocytes	Polymorphs	Eosinophils	Total Granulocytes
Dec. 5 ..	2,600	4%	13%	442
,, 6 ..	4,300	6%	8%	602
,, 7 ..	4,000	10%	3%	520
,, 8 ..	5,500	15%	7%	1,210
,, 9 ..	4,400	17%	4%	924
,, 10 ..	8,800	14%	9%	2,024
,, 11 ..	7,000	36%	4%	2,800
,, 12 ..	7,150	35%	8%	3,074
,, 15 ..	9,350	46%	6%	4,862
,, 20 ..	8,000	60%	2%	4,960

On Dec. 6 the staphylococcus obtained from his lesions wa reported to be penicillin-resistant. The dose of penicillin wa immediately doubled. At this time, though his temperatur had subsided and his general condition was excellent, the bucca ulcer was showing no signs of healing. During the next fe days this situation was reversed and the ulcer healed steadily

It will be seen that restitution of the blood picture wa delayed, and it seems reasonable to assume that this wa

related to the fact that the infecting organism proved relatively resistant to penicillin and that it was not subjugated until the dosage was considerably increased. This patient received in all 15 mega units of penicillin.

Discussion

In this small investigation it appeared that infection was playing the major part in the aetiology of the condition, and that its control allowed recovery of the bone marrow, a recovery which further arsenic was unable to prevent.

In other conditions associated with granulopenia I have noticed serious deterioration as a result of superadded infection. A man convalescent from glandular fever sustained a streptococcal infection of his throat. His polymorphs promptly fell from 1,800 to 90 per c.mm., to rise again immediately the infection had been subdued by penicillin. A woman suffering from chronic lymphatic leukaemia developed gross infection in her mouth and throat. This resulted in a grave illness, with high fever, widespread purpura, and a rapid fall in the haemoglobin level, which reached 25%. Treatment with parenteral and intraoral penicillin rapidly overcame the infection, the fever fell to normal, the mouth lesions healed, the purpura vanished, and the haemoglobin began to rise, eventually reaching over 100%. She has remained well during six months' subsequent observation, though her blood picture is still, of course, that of chronic lymphatic leukaemia. In other cases of leukaemia acute and threatening episodes have been initiated by sepsis, the control of which has resulted in temporary improvement in the patient's condition.

There seems to be little doubt that a functionally damaged bone marrow is particularly vulnerable to the toxins resulting from sepsis. It is well known, for example, that infection can interfere with the full therapeutic effect of liver extract in the treatment of Addisonian anaemia.

The factors giving rise to neutropenia are doubtless multiple. In addition to the part played by leucotoxic drugs—and no one will challenge this factor—it seems that idiosyncrasy, sensitization, age, sex, and endocrine factors must all be taken into account. But it may well be that infection, which is, I believe, the only factor common to almost every case, is the most important of all. A recognition of this possibility is clearly of considerable therapeutic and preventive importance. It would seem wise to exclude sepsis in cases of rheumatoid arthritis and thyrotoxicosis before embarking upon treatment with gold or the thiouracils. At the same time patients undergoing treatment by any of the recognized leucotoxic drugs should be warned to avoid infection and to report the smallest infective process immediately. Printed instructions might be valuable from this point of view. It is doubtful if the white cell count is of any value in giving warning of white cell depression, and may even lead to a false sense of security.

It has always been said that the appearance of a blood dyscrasia while undergoing treatment by any of these drugs precludes for ever the use in such a patient of the particular material thought to have been causative. The observations recorded here suggest that this dictum may not need to be adhered to when there are indications for further administration of the offending preparation. McGibbon and Glyn-Hughes (1943) came to the same conclusion after describing a case of agranulocytosis following arsenic.

In 1942 a fulminating case of agranulocytosis under my care, following the use of sulphapyridine, was given after recovery 3 g. of the drug by intravenous injection. Frequent white cell counts made during the subsequent 48 hours revealed no fall in the number of granulocytes.

Conclusions

It is suggested that in conditions of serious neutropenia infection plays a predominant part; that in its prevention, while undergoing treatment with possibly leucotoxic drugs, avoidance of infection, both endogenous and exogenous, is of more importance than repeated blood examinations; and that in the treatment of the established condition attention should be centred upon the immediate arrest of the infective process by the free use of the most suitable specific drug, which at present is likely to be penicillin in most cases. It should be given in large doses, in the region of 1 mega unit daily. In these circumstances pentide, blood transfusion, etc., may with advantage be withheld during the first 72 hours. If there has been no response at this stage pentide should be started and continued until response is well established. Fresh blood, folic acid, pyridoxin, ascorbic acid, liver extract, and thyroid may all be useful in individual cases. Where there has been satisfactory response to penicillin alone it may be possible to resume the supposedly leucotoxic drug, if necessary.

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INSTRUCTION OF THE MEDICAL STUDENT IN PAEDIATRICS

AN INSIGHT INTO FAMILY PRACTICE

BY

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Instruction of the medical student is concerned primarily with the training of the future family doctor. Undergraduate training suffers from having to be provided under conditions dominated by hospital considerations of disease. As a result the recently qualified doctor entering general practice has to adjust his outlook. He is not long in practice before he realizes that many of the problems which appeared simple of solution when seen in hospital are complex when considered in relation to the needs of the home. Short of restoring the old-time apprenticeship system it is difficult to see how this handicap can be completely offset.

The handicap applies particularly to undergraduate study of health and disease in infancy and childhood. Ward instruction is deficient because of the absence of the mother and of any visual reminder of home conditions. The

deficiency is made good in part, but only in part, by teaching in hospital out-patient departments, at infant-welfare sessions, and at school medical inspections. These sessions, no matter how efficiently they are run, are apt to suffer from a routine intended to cope with a considerable number of children in a set period of time. Health and disease in childhood are studied in an atmosphere of organized efficiency rather than one of intimacy of understanding. The student is left with an impression of a limitless tide of "cases," some of interest, others of doubtful interest. The tide is apt to flow with such speed that in his concern over physical findings the student is insufficiently impressed by the human family problem presented by each child. Nor can the hospital clinician, be he ever so able a teacher, convey to the students that full depth of understanding of mother and child and family circle which makes for successful care of child life in general practice.

Experiment at Leeds

The medical student taking out his course of clinical instruction in paediatrics and child health at the University of Leeds is given opportunities of seeing healthy and ailing children in hospitals and at clinics, handicapped and "deprived" children in day and residential homes, and some of the homes from which sick children have been admitted for treatment in hospital wards. In the course of his studies the same student meets practitioners on the visiting staffs of hospitals and in the employ of local authority child-health services, nurses working in hospital or as health visitors, school nurses, and district nurses or district midwives. He is given a didactic lecture by a family doctor on the theme of paediatrics as met with in general practice, but until recently has not seen the family doctor at work.

We are convinced that the family doctor has a vital part to play in care of the child in health and disease. We are equally convinced that training of the future doctor in paediatric care would derive immeasurable benefit from early insight into such care as is provided in the course of everyday general practice. Ourselves (W.S.C. and F.C.N.) brought up from childhood in the households of family doctors, we are acutely aware in our professional work to-day of the debt we owe to that privileged experience of the past. Over a number of years one of us (F.C.N.) has made a special study of infants and children seen in the course of day-to-day family practice. Study pointed to the desirability of expanding the range of service offered to mothers and children in practice. One way in which expansion was developed was to reserve an afternoon each week for consultations for mothers and their children. In effect a clinic was established as an integral part of the activities of the family practice. The clinic proved a success from the start and has now run uninterruptedly for almost two years. There is implied recognition of its value in the authority recently given by the local executive council to continue the established policy of reserving one afternoon each week for mothers and children.

We felt that the training in paediatrics of the future general practitioner would benefit by insight into the work of a clinic conditioned by the circumstances of family practice. Experimental arrangements were therefore made to enable students, while attached to the University Department of Paediatrics and Child Health, to visit the clinic. We are satisfied that the arrangements have proved their value. The purpose of this paper is to give an outline of the arrangements and their results, because it is considered they indicate means whereby undergraduate, and indeed postgraduate, instruction of the medical student can be widened and improved.

The General Practice

The practice is one of a number in a non-university city with an approximate population of 100,000. The bulk of the work is concerned with the families of manual labourers, clerical workers, and shop employees. Of other persons on the practice list a small number are members of professional and military families. Midwifery constitutes an important part of the activities of the practice, and in the matter of social groups reflects the distribution characteristic of the practice as a whole.

The Clinic

The clinic is held in the family doctor's private house, which is situated in a working-class district. Accommodation consists of a weighing-cum-secretarial room, a waiting-room, and a consulting-room with screened examination couch. The accommodation is in fact the "surgery." Furnishings include low seats suited to use by nursing mothers.

Sessions are held weekly. The family doctor (F.C.N.) has the assistance of a secretary and nurse, and has recently been offered the services of a health visitor by the maternity and child-welfare authority. Attendance is on a voluntary basis and by appointment. Mothers who attend with their babies consist of those delivered by the doctor, of those who are on the doctor's National Health Service list but who have been delivered in hospital or by a midwife, and a few referred by the doctor's partners in the family practice. Of newly born infants in the practice approximately 80% attend the clinic. Mothers are advised to attend weekly until the baby is 3 months old, fortnightly during the next three months, and thereafter at monthly intervals until the baby reaches his first birthday. Older children attend at longer intervals or at any time, prior to school age, when their mothers wish advice on account of any difficulties in upbringing.

Attendances average twenty-six a session. All children are weighed, and individual records are kept on separate cards. Duplicate cards are kept by the mothers. At any one session rather more than 50% of those attending are seen personally by the doctor at the request of the mother, at the instigation of the nurse, or in accordance with arrangements made by the doctor at the time of a previous visit.

Work of the Clinic.—The ages of children attending range from a few weeks to 5 years. Infants predominate. All children are accompanied by their mothers, who know that they must not bring any child thought to be incubating or harbouring infection. It is one of the objects of the clinic not to divorce care of the infant from care of the mother or family. Health and disease are not arbitrarily differentiated. General management, the promotion of health, and the prevention of disease receive equal attention. The indications for consultations arise from an infinite variety of circumstances. They include comprehensive routine inspections; the supervision of infant feeding, whether breast, complementary, or wholly artificial; attendance for vaccination or immunization; requests for advice concerning symptoms which, were there not a clinic, might be ignored; family problems such as those arising from ill-health of the mother or from enuresis on the part of the child; and social problems such as those concerned with adoption and illegitimacy.

Arrangements for Medical Students

Attendance at the clinic is entirely voluntary. Provision is made for three students accompanied by a registrar (M.F.G.B.) to be present at each session. A number of

factors, including those related to distance and transport, make it impossible to arrange for any one student to be present at more than one session. At the time of his visit the student is encouraged to discuss the individual problems he has seen and any general considerations which particularly interest him.

All students have taken advantage of the opportunities offered them. They know they are taking part in an educational experiment. No attempt has been made to influence them in their views, and particular care has been taken not to initiate comparisons concerning different services for the care of child life. The students have willingly co-operated when asked after their visit to give a written account not so much of their impressions concerning detail as of their reactions to inclusion of the visit in the course of their training.

The Student's Reaction

A point of practical importance is that at no time has there been any unfavourable reaction to the presence of students on the part of mothers attending the clinic. As to the students themselves, while some few were constructively critical of certain aspects of the arrangements made for them, all testified to the value of their visits to the clinic. Many were unreservedly enthusiastic. Significance attaches to the reasons given for their opinions.

Almost all the students stressed that the visits had given them their first opportunity to "see general practice in operation." Of those who made this comment a number wrote of having appreciated for the first time the part which the family doctor can play in the care of child life in health and disease. Reading their remarks, it is evident that a number of students had had borne in on them how many of the children they see in the hospital out-patient department could be properly dealt with in the more suitable environment of a family doctor's consulting-room. Others, again, were impressed by seeing conditions which are rarely encountered in hospital but which, although they may have no serious immediate clinical significance, bulk more largely in general practice.

Most of the students remarked upon the advantages to child care of the mutual understanding and trust which it is within the power of the general practitioner to establish with the families he attends. Other students appreciated the initial advantage possessed by the family doctor whose care of children starts in the form of antenatal supervision of the mothers and who knows the background and capabilities of families in his practice. A number of students, men and women, sensed the benefits to infant feeding of supervision being undertaken by a doctor herself the mother of a family. Women among the students realized that marriage and a family do not necessarily debar a woman from making a vital and special contribution to child care in general practice.

We consider that the various views expressed by those visiting the clinic support the opinion that the experiment has justified itself. Evidence in favour of this opinion is to be found from the following extracts from notes sent in by three of the students who have taken part in the experiment. Telling of his outlook before visiting the clinic, one student wrote: "As a medical student one of the impressions I had conceived of general practice was that any case which required a little more trouble taken over it than normal was immediately referred, especially in paediatrics, to the already overworked hospital."

Another student wrote: "It [the visit] helped my sense of proportion in realizing the great value of the general practitioner in the promotion of child health." A third student summed up his impressions as follows: "The visit made me realize that general practice is not static and can be made progressive . . . and can provide intellectual satisfaction."

Summary

Measures for the care of child life must be based upon the home. The family doctor has a vital part to play in any such measures. If it is to fulfil its primary function medical training of the undergraduate must be directed towards preparation for family practice. Teaching instruction in the care of child life is handicapped by difficulties in the way of giving the medical student practical insight into conditions prevailing in family practice.

An educational experiment is described which is intended to offset these difficulties in part at least. It is considered that the experiment has been a success, is capable of further development, and might be extended to a wider field of medical training than that concerned solely with health and disease in childhood.

INTERMENSTRUAL PAIN (THE "MITTELSCHMERZ") AND THE TIME OF OVULATION

BY

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(From the Department of Anatomy, the Medical School, Birmingham University)

Cyclically recurring pain in the pelvis which can be related to the phases of the menstrual cycle is not uncommon in women. The condition was described by Priestley as long ago as 1872, although it is just possible that his observations were confused by the coexistence in his patients of chronic appendicitis, which at the time he wrote had not been defined as a clinical entity. Subsequent reports, in which corresponding pelvic pains have been referred to, mainly concern acute conditions that have called for operation, and in many instances laparotomy at the time of the pain has disclosed a recently ruptured ovarian follicle.

The periodicity of intermenstrual pelvic pain is one of the many signs that have been taken to indicate the time of ovulation in women. In view of the very clear-cut symptoms over a long period it is of interest to report the following case history.

Description of Present Case

The patient is a married woman aged 28 in whom cyclical intermenstrual pain has been recorded without interruption during the last 4½ years. It has occurred over at least seven years, but at first it was irregular. She has no recollection of similar pains before the age of about 16.

The pain is characteristic and easily recognized. It lasts for no more than 24 hours, and varies somewhat in intensity from time to time. It is never severe and can be controlled with simple analgesics. It begins suddenly in one or other iliac fossa and is gradually referred to the pubes, from which it spreads as a generalized pelvic pain.

The occurrence of the pain and the menstrual periods from April, 1944, to November, 1948, are charted in Fig. 1. The Table shows the duration of the two "phases" of the cycle. The following points may be noted.

Table Showing Distribution of Duration of Phases of Menstrual Cycle

	Duration in Days												
	10	11	12	13	14	15	16	17	18	19	20	24	25
1st day of menstruation to mittelschmerz					1	6	8	13	6	4	2	2	2
Mittelschmerz to onset of menstruation	1		10	22	7	1	1						

1. The onset of the pain is regular. The mean interval from menstruation to the onset of the pain is 17.3 ± 0.33 days, and from the pain to the beginning of menstruation 13.0 ± 0.15 days. In agreement with most other statistics on the duration of the pre-ovulatory and post-ovulatory phases of the menstrual cycle, the second phase has a significantly smaller variance than the first pre-ovulatory phase (see Table). Although the length of one of the later cycles was prolonged to 39 days, the mittelschmerz occurred as usual 13 days before the next period. Presumably the extra length of the cycle was due to some interference with normal follicular development.

2. In July, 1944, the patient wished to become pregnant and was advised to regard the mittelschmerz as the most likely indication of the time of ovulation. Ten days after the mittelschmerz in that cycle, and before the next period was due, the patient correctly believed that she was pregnant. No further pains were noted during either her pregnancy or her lactation. About three weeks after the end of lactation the pain was again recorded, and was followed ten days later by the return of menstruation. Since then it has continued its regular rhythm without interruption.

3. The pain has occurred 29 times on the right side and 14 times on the left. This predilection for the right side is significantly different from a 1 : 1 ratio for the two sides. Similar differences in favour of the right side have been reported for ovulation in the sheep (McKenzie and Terrill, 1937) and the monkey (Morse and van Wagenen, 1936), and, assuming that the pain indicates ovulation, the observed ratio in this case does not differ significantly from the figures reported by these workers. There does not seem to be any regularity of alternation from left to right side. The pain has never occurred twice in one cycle.

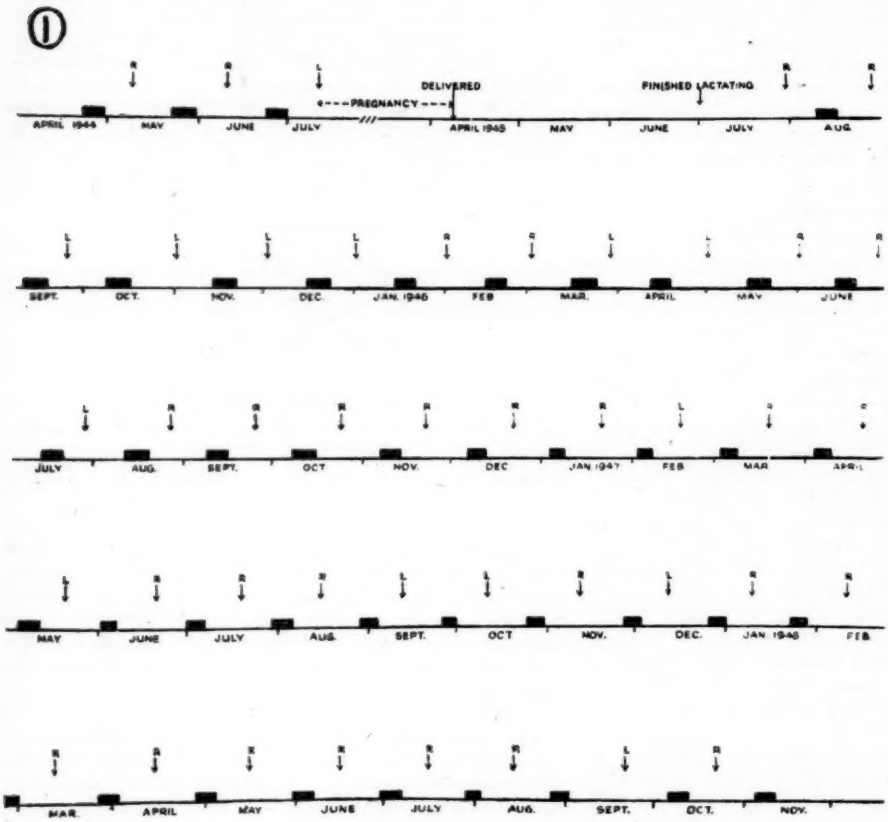

FIG. 1.—Menstrual cycles from 1944 to 1948. Occurrence and side of mittelschmerz are indicated by the arrow and R or L.

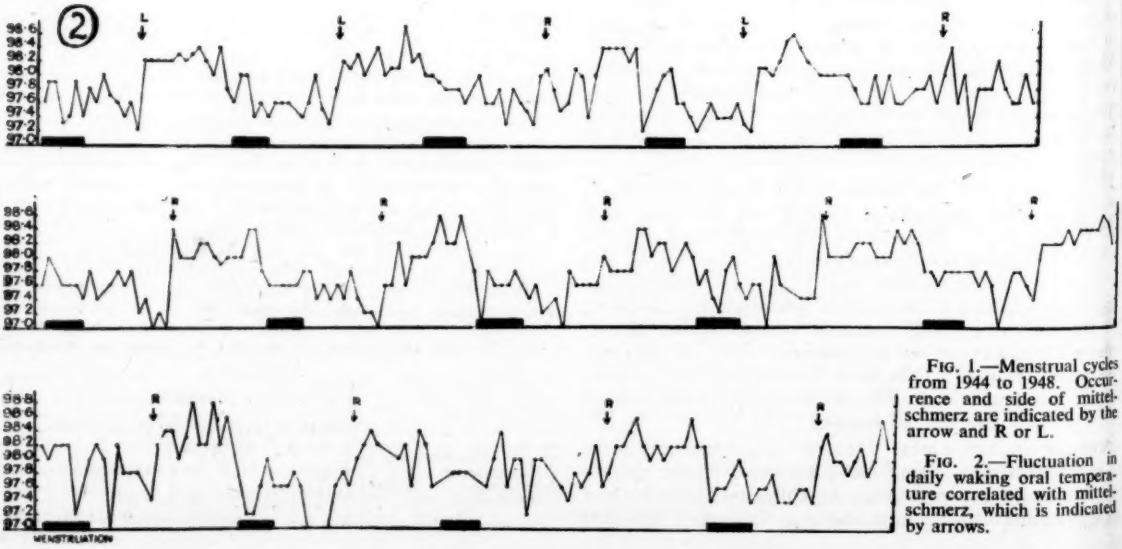

FIG. 2.—Fluctuation in daily waking oral temperature correlated with mittelschmerz, which is indicated by arrows.

Correlation of Mittelschmerz with Fluctuations in the Waking Oral Temperature

Since fluctuations in the body temperature are now widely used to indicate the time of ovulation a record of the daily waking oral temperature has been kept for the last 13 cycles. The results are plotted in Fig. 2, the mittelschmerz being indicated by arrows.

The temperature recordings conform in general to the usually accepted pattern, though they are not so clear-cut as some that have been published. In the middle of the cycle, however, there is usually a slight fall in temperature, followed by a steep rise to a plateau, which is maintained until near the onset of the subsequent period. Occasionally this rise is indistinct.

An independent observer was asked to estimate the most likely time of ovulation from temperature charts alone. In eight of the 14 cycles ovulation, as judged in this way, agreed with the day of onset of the mittelschmerz. In three cycles the estimate was one day early, and in three it was one day late.

A change in the temperature curve, particularly when the whole chart is available and when attention is directed to the mid-cycle, is at best only indirect evidence of ovulation, but the close relation between the temperature change and the mittelschmerz is of interest.

Discussion

Early workers who described the mittelschmerz were in difficulties in ascribing a cause to the pain. This was due primarily to the fact that ovulation was thought to be closely related temporally to the onset of menstruation. It is now known from both direct and indirect evidence that ovulation occurs at some moment in the middle of the cycle. Intermenstrual pain, like changes in hormone excretion in the urine, physical changes in the cervical mucus, electrical potential changes, and so on, is obviously an indication of some alteration in the reproductive tract, and may be accepted as further evidence that ovulation occurs in the middle of the cycle.

The cause of the pain is still obscure. It is abolished by ovariectomy, but is not affected by operations that interfere with nervous pathways from the uterus. Painful tubal contractions may, however, be a possible explanation.

If, as the evidence suggests, the pain is connected with ovarian changes, the immediate cause may be either the pressure of a distending follicle just before ovulation or the actual rupture of the follicle.

It seems probable that the pain gives a closer indication of the time of ovulation in those women who are aware of it than any other method. In view of the experience of McSweeny and Wood (1940) that 21 out of 134 women could identify some discomfort in the mid-cycle, careful questioning about the mittelschmerz of patients who attend fertility clinics would seem to be worth while. Cases have certainly been reported (Wharton and Henriksen, 1936) in which the pain had been severe enough to prevent intercourse and in which advice to disregard the pain was immediately followed by conception.

Summary

The cyclical occurrence of intermenstrual pain (mittelschmerz) has been followed for 4½ years in a married woman aged 28.

The onset of the pain is closely correlated with changes in the waking oral temperature, and is taken to be a reliable index of ovulation.

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SYNDROME OF DIAPHRAGMATIC HERNIA AND ANAEMIA

BY

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No medical or surgical disease presents a clinical symptomatology so varied and unstable as that of congenital or acquired diaphragmatic hernia. Harrington (1945) studied 320 cases of oesophageal hiatus hernia and found that an average of three previous erroneous diagnoses had been made before the correct diagnosis was established. In order of frequency the most common erroneous diagnoses were: cholecystitis, cholelithiasis, gastric ulcer, secondary anaemia, duodenal ulcer, hyperacidity, cardiac disease, carcinoma of the cardia, stricture of the oesophagus, appendicitis, and intestinal obstruction. Chevallier and Danel (1944) reported that diaphragmatic hernia was commonly associated with anaemia.

Katsigras (1946) reviewed the published reports of 955 cases of oesophageal hiatus hernia and observed that anaemia was associated with the hernia in 80 cases, a proportion of 8.3%.

In my view (Codounis, 1946) diaphragmatic hernia can provoke the appearance of microcytic or hypochromic anaemia, or of macrocytic or hyperchromic anaemia. The personal case here described appears to be unique in medical literature. A severe anaemia persisted for 24 years, as did the diaphragmatic hernia. At first there was a microcytic anaemia and later macrocytic anaemia.

Case Record

J. A., a man of 60, had previously suffered from malaria and jaundice. He had three children in good health, two born after the beginning of the anaemia. His present illness started in April, 1922. After an emotional disturbance he had been feeling increasingly weak, tired, and anxious. His skin was pale and his eyes yellowish. These symptoms, with anorexia and loss of weight, became more serious, and he consulted Professor Schlesinger in Vienna, who diagnosed hypochromic anaemia and prescribed iron and a change of climate.

Phase of Microcytic Anaemia.—After three months' rest at Semmering J. A. returned feeling better. In December, 1922, pallor and progressive weakness reappeared, with vomiting, nausea, and epigastric swelling after meals. In February, 1923, he went to Vienna to consult Dr. Eppinger, who diagnosed Banti's disease and advised splenectomy. *X*-ray examination of the gastro-intestinal tract revealed no abnormality—probably due to a technical defect.

J. A. later went to France, where the diagnosis of hypochromic anaemia was confirmed. After four months' rest in the country he came home in good health and noticed no symptoms during the year 1923.

In 1924, after the same clinical and haematological symptoms and some loss of weight (100 kg. to 82 kg.), he returned again to France and consulted Dr. P. E. Weill, who confirmed the diagnosis of hypochromic anaemia. The patient was given iron and liver extracts, which improved his condition. His red cell count fell to 3,000,000 per c.mm. in 1925, and Dr. Weill gave him a blood transfusion, after which the improvement was nearly complete. Between 1926 and 1938, during which twelve years he had iron therapy and a change of air each summer, the patient was free from symptoms and lost no more weight. His usual weight was 100 kg., which was considered normal in relation to his height.

After an attack of influenza in November, 1938, J. A. felt very weak and dizzy. There was marked pallor of the skin

and mucous membranes, and a generalized oedema. Iron and liver extracts were prescribed and he was given three blood transfusions; the second provoked a severe anaphylactic shock, which was nearly fatal. Five days later the red cell count was only 900,000 per c.mm. Slowly the anaemia improved again; large doses of iron, 10 to 12 g. daily, were prescribed, but the patient could take only 4 to 5 g. daily.

He felt no pain between 1939 and 1941, but because of wartime food shortages he lost 25 to 30 kg. in weight.

In July, 1941, apart from weakness and pallor, J. A. complained of pains in the left upper abdomen and palpitations. Dr. Maroulis, a colleague who saw him during this period, noted besides the anaemia hyperresonance in the left chest. The same iron therapy was continued and the patient improved again over the next five years (October, 1945).

Altogether the evolution of the first phase of microcytic and hypochromic anaemia included three long periods in which the condition was absolutely quiescent; after the appearance or reappearance of symptoms improvement was brought about by treatment with iron, and the patient could live a normal life.

Phase of Macrocytic Anaemia.—Marked pallor and oedema reappeared in November, 1945, together with pain in the left upper abdomen radiating to the scapular and lumbar regions. A blood count showed: r.b.c., 4,120,000; w.b.c., 6,400; Hb, 70%; colour index, 0.85. His symptoms grew rapidly worse, however, and on Dec. 26, 1945, J. A. came under my care.

At that time his temperature was 38.4° C. (101.2° F.), pulse rate 80, and he had slight tachypnoea. His face was like that of a case of nephritis, oedematous and very pale. His lips were bloodless, he was very weak and, besides the puffiness of the face, there was marked oedema of legs and meteorism. He had a slight thoracic kyphosis. His chest was of the emphysematous type; the percussion note was tympanitic; rales were heard at both bases.

Blood pressure: 170/90 mm. Hg. *X*-ray examination of the chest and heart indicated no abnormality. Radiographs of the spine revealed changes in the third and fourth dorsal vertebrae, probably due to a healed spondylitis. Examination of the urine showed some white cells and some calcium oxalate crystals.

Final Diagnosis

With this history and the findings here tabulated it was easy to assume a relapse of the anaemia which had affected the patient for 24 years. But we were surprised to see that instead of a microcytic and hypochromic anaemia there was a macrocytic and hyperchromic anaemia. Then, on Jan. 5, 1946, an *x*-ray examination by Dr. Xanthakis,

TABLE I.—*Haematological Findings*

Date	R.B.C. End of Microcytic Phase	Hb %	Colour Index	W.B.C.	Differential Count %			
					Polymorphs	Lympho.	Eosino.	Mono.
7.11.45	4,120,000	60	0·85	6,400	60	32	4	4
Macrocytic Phase								
27.12.45(A)	1,880,000	37	1·02	8,600	50	46	—	4
5.1.46	2,440,000	50	1·04	—	—	—	—	—
7.1.46	2,770,000	50	0·92	—	—	—	—	—
11.1.46	3,080,000	43	0·70	8,400	78	22	—	—
14.1.46(B)	2,540,000	46	0·72	6,000	66	28	4	2
15.1.46	3,000,000	45	0·75	—	—	—	—	—
21.1.46(C)	3,430,000	52	0·76	7,000	62	34	2	2
30.1.46(D)	3,040,000	55	0·91	5,200	56	38	2	4
2.3.46	3,660,000	65	0·90	4,600	66	22	8	4
6.3.46(E)	4,480,000	75	0·85	5,000	66	28	4	2
Phase of Relapse								
29.3.46	4,000,000	70	0·87	—	69	25	3	3
1.4.46	3,800,000	72	0·94	—	78	16	2	4
4.4.46(E)	3,120,000	—	—	—	—	—	—	—
5.4.46	1,850,000	35	0·94	12,000	—	—	—	—
8.4.46	1,030,000	17	0·82	18,400	—	—	—	—

A. Evidence of polychromasia, anisocytosis, poikilocytosis, and predominance of macrocytes—among them are ovular and well-coloured macrocytes (Naegeli's megalocytes). No granular erythrocytes. Some white cells with globular nuclei.

B. Average anisocytosis and poikilocytosis and hypochromia. Predominance of macrocytes and among them some Naegeli's megalocytes. Some giant platelets.

C. Average hypochromia and anisocytosis and poikilocytosis. One acidophilic normoblast per 100 white cells.

D. Some polychromasia, slight anisocytosis and poikilocytosis.

E. Bleeding time, 3 minutes; coagulation time, 9 minutes; blood urea, 0.45%; 380,000 platelets.

TABLE II.—*Bone-Marrow Picture*

Reticulo-endothelial Series	I	II	III
	%	%	%
Reticulocytes	4	2	13
Endothelial cells	2	2	3
Fatty cells	—	—	—
Erythroblasts:			
Proerythroblasts	5	2	2
Basophilic erythroblasts	12	6	1
Polychromatophilic erythroblasts	8	34	85
Normoblasts	10	37	12
Megaloblasts	8	—	—
White cells:			
Myeloblasts	2	2	2
Promyelocytes	5	4	6
Myelocytes	7	12	25
Metamyelocytes	10	20	15
Rod cells	15	17	16
Polynuclear cells	50	31	18
Eosinophilic myelocytes	1	—	1
Eosinophilic polynuclears	1	—	1
Basophils	1	—	—
Monocytes	1	—	—
Lymphocytes	1	7	—
Ferrata cells	—	1	—
Platelets:			
Megakaryocytes	—	2	—

I.—Dec. 27, 1945. Mitosis chiefly among the basophilic erythroblasts and anisocytosis with predominance of Naegeli's macrocytes. Vacuoles in the protoplasm and in the cellular nuclei.

II.—Jan. 17, 1946. Normoblasts present with relatively few mature nuclei in comparison with the protoplasm. Mitosis. Rods of giant cells and a good number of cells with lobulated nuclei.

III.—Immediately after death on April 10, 1946. Majority of reticulocytes are of Ferrata type. Majority of nuclei of polychromatophilic erythroblasts are in mitosis. Macroblasts rarely found. Asynchronism in maturation. Immature megakaryocytes noted with basophilic protoplasm and without lobulation of the nucleus.

undertaken to exclude the possibility of gastric ulcer or cancer, explained clearly the anaemia and the digestive symptoms and thoracic pains.

Immediately after the patient had taken the barium meal a displacement to the right of the lower end of the oesophagus was observed. A large pocket of air in the herniated and distended stomach extended seven finger-breadths above the diaphragm. The stomach was elongated, and immediately below the diaphragm, on the lesser curvature, a diverticulum was noted. Another small diverticulum was observed in the descending part of the duodenum. Here then was a case of diaphragmatic hernia in a man who had been treated for anaemia for over twenty-four years. This is the fortieth case of this syndrome to be described in the literature and the first case to be observed in Greece up to April 16, 1945, when a preliminary communication was made to the Medical Society of Athens. Reviewing the long history of this case, it may be seen to fall into six successive stages.

Stage 1.—Apparently perfectly healthy until the age of 36.

Stage 2.—Onset of hypochromic anaemia, from 36 to 39 years of age. It is at this stage that J. A. complained of the first dyspeptic disturbances—post-prandial discomfort, epigastric fullness, and occasional vomiting. Over these four years improvement in the anaemia would be followed by recrudescence, followed again by rapid improvement.

Stage 3.—The twelve years from the age of 39 to 51 are characterized by almost normal good health.

Stage 4.—From the age of 52 to 54 there was a new and intense recrudescence of anaemia, following a severe attack of influenza in 1938. He lost 25 to 30 kg. in weight and his red cell count fell to 900,000 per c.mm. Later, on consulting the patient's wife, we were told that at this period she heard some gurgling in his stomach, even at some distance away from him. At the same time he complained of acute pains in the left hypochondrium, disappearing a few minutes after protracted belching. Physical examination at that time showed a pronounced hyperresonance of the left hemithorax.

Stage 5.—Quite well again from 55 to 60 years of age.

Stage 6.—The final stage lasted six months, and coincided with a hyperchromic and macrocytic anaemia.

In our opinion this hernia was congenital, favoured by the patient's kyphosis, and it progressively dilated through

the diaphragmatic hiatus over a period of 24 years and was responsible for provoking the alternating anaemic syndrome. Diagnosis in these cases is extremely difficult. Often a secondary anaemia due to cancer is suspected, but an *x*-ray examination reveals the diaphragmatic hernia instead of cancer. This was true with our case as with the cases of Welti and Mahoudeau (1948). The discovery of a diaphragmatic hernia must often lead to surgical intervention. In fact, according to Welti and Mahoudeau, the only effective cure is surgical. In addition, the results of operation prove that the diaphragmatic hernia is the cause of the anaemia, since the latter disappears after operation.

Cause of the Anaemia

To explain the mechanism of this anaemia, Anglo-Saxon authors have invoked repeated haemorrhages. But in our case, and in many others, analysis of the stools has not revealed the least evidence of melaena. Chevallier (1944) suggested that the anaemia might be due to atrophy of the gastric mucosa and gastric achylia. Chevallier could not determine this point in his case, and the same applied to J. A. We tried several times to withdraw gastric juice, but failed to do so because of the extreme nervousness of the patient. Nevertheless, it was possible to withdraw gastric juice from another patient of approximately the same age and with a diaphragmatic hernia. This showed a complete achylia, even after the caffeine test. This patient, in spite of his pronounced emaciation and severe illness, paradoxically does not show any anaemia. His red cell count was 4,200,000 per c.mm., with haemoglobin 100%.

It is the fact that a proportion of cases of diaphragmatic hernia show some degree of anaemia. In most cases this is a microcytic hypochromic anaemia responding as rapidly to iron therapy as to surgical treatment of hernia. Hyperchromic macrocytic anaemia is very rare in these cases. Only one case was mentioned by Cain and his collaborators (1939), with a colour index of 1.50 and a severe hyperchromic and aplastic anaemia. This hyperchromic macrocytic anaemia has nothing in common with Biermer's anaemia. The anisocytosis is not accompanied by megalocytosis but by normoblastosis and macrocytosis, although to-day, according to some authors, megalocytosis and macrocytosis are almost synonymous. This anaemia also presents a distinct resemblance to that of avitaminosis B_1 and B_2 and to certain other primitive or secondary anaemias. In the case described by Cain liver therapy proved ineffective, whereas cure was effected by gastric extracts.

In the macrocytic stage in our patient liver extracts and small direct transfusions of fresh blood over 27 days raised the red cell count from 1,800,000 to 3,430,000 per c.mm. and notably improved the myelogram (see Table II). The improvement was remarkable, both clinically and haematologically.

In the 44 days following admission our patient received 350 ml. of fresh blood (by direct transfusions), 48 g. of iron, and 78 ml. of liver extract (by intramuscular injection). Clearly our patient needed not only anti-anaemic factor but also iron, owing to the presence of alternating microcytic and macrocytic anaemia.

Crisis and Death

After his discharge on March 6, 1946, with 4,180,000 red cells per c.mm., the patient remained well only until March 15.

He then began to feel slight pains in the left hemithorax and in the abdomen, which from time to time was distended. These pains were intermittent, and were relieved by belching. On March 30 the patient complained of severe pains in the right and left chest. At the same time he presented pallor, anorexia, insomnia, and extreme asthenia.

On March 31 he was much worse and was readmitted. The radiologist's examination showed that the intrathoracic gastric pouch seemed more voluminous. There was also a gross distension of the ascending and transverse colon, displacing the liver to the left. We were obliged to assume that a sudden dilatation of the intrathoracic hernial pouch due to fermentative gases had provoked diaphragmatic spasms at the level of the oesophageal hiatus, which, by exciting the vago-sympathetic system, affected in turn the abdominal segment of the stomach as also the small and large intestines.

These spasms, being repeated, disturbed the function of the digestive tract and respectively, by compression, the circulatory and respiratory functions. It is possible that this spasm contributes (by a mechanism which we have still not explained) to the production of putrefaction and fermentation (given the existence of an obstinate constipation), and so to the dysfunction of the haematopoietic system. In a case of this nature it may be that haemolytic factors discharged by the digestive tract into the circulatory system contribute to the production of this kind of anaemia. In any case, this last stage of severe anaemia was provoked from the second day by an intense hernial crisis simulating a strangulation. Once and only once we noted a positive Meyer's reaction in the faeces after an enema. There had been such obstinate constipation that we were obliged to extract the faeces digitally, and this probably caused small anal erosions which would explain this positive reaction.

We claim that this stage of the disease in our patient furnished indisputable proof that a diaphragmatic hernia can provoke an anaemia so severe that it may lead, with or without strangulation, to a fatal issue. On the eleventh day of this intense crisis J. A. died. We regret to say we could not proceed to necropsy owing to the objections of the relatives.

Conclusion

During the evolution of any form of diaphragmatic hernia different anaemic syndromes can occur. These ordinarily take the form of a microcytic or hypochromic anaemia—rarely the hyperchromic or macrocytic anaemia; and sometimes these syndromes alternate, as in our case.

In any case of anaemia in which the aetiology is not known a complete *x*-ray examination should not be omitted. This may reveal a diaphragmatic hernia. Conversely, whenever a diaphragmatic hernia is found we should not neglect a complete study of the patient's blood and bone marrow.

Summary

A case of diaphragmatic hernia is described in which a long-standing microcytic anaemia was succeeded by a severe and ultimately fatal macrocytic anaemia.

I am indebted to the Director of the laboratory of the Red Cross Hospital, Dr. S. Papageorgiou, for his help in the detailed study of the blood and the bone marrow.

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The Ministry of Health has issued a circular drawing the attention of hospital management committees and boards of governors to the importance of close liaison with the resettlement services of the Ministry of Labour. During the war the Ministry of Labour set up a staff of disablement resettlement officers to give advice and assistance on the employment of disabled people who have difficulty in getting or keeping a job. In many cases the disability was mental or complicated by mental factors. This service will now be extended as widely as the mental health resources of the National Health Service permit. The Ministry hopes that psychiatrists and D.R.O.s will get into personal touch with each other and co-operate in working the scheme.

AMOEBIC VAGINITIS

BY

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Amoebic vaginitis is rare. In a study of 200 cases of leucorrhoea Bickers (1943) observed that 0.5% were due to *Entamoeba histolytica*, but he did not report any case. Between 1916 and 1948 only fourteen cases have been recorded, notably by May (1943), Morse and Seaton (1943), Cleland (1944), de Rivas (1944), Weinstein and Weed (1948), and others. Most textbooks are silent about a condition which should receive more attention, particularly in the Tropics and subtropics, where the incidence of amoebic infestation is fairly high.

Case Report

A nulliparous Nepalese widow, aged 35, was seen in May, 1948. She complained of a profuse seropurulent vaginal discharge first noticed in January of that year. There was some soreness of the vulva and a slight burning sensation in the vagina and during micturition. The discharge was almost continuous, and there was no alteration in its character or amount before or after menstruation.

She had had a severe attack of dysentery, presumably amoebic, in December, 1947, when she was treated elsewhere and no specific remedy was administered. Soon afterwards she noticed swelling and pain in the perineum and the lower parts of both labia majora. The present symptoms followed and the discharge increased until she was forced to come to the hospital for treatment.

Pelvic examination had to be undertaken under general anaesthesia. The lower part of the right labium majus was slightly swollen. The fourchette presented a small ulcer in its right half. In the vagina there were many linear ulcers, lying mostly transversely in the furrows between the folds of mucosa. They were superficial, punched-out ulcers with slightly overhanging edges which bled easily. The bases were raw and red except for a few ulcers near the fornices covered with a thin yellowish slough. The cervix was slightly enlarged, soft, and ulcerated over the whole of its surface except for a small rim near the reflection of the vaginal mucosa on the portio. The external os could not be detected. The uterus was bulky, soft, and anteverted.

Examination of the thick seropurulent vaginal discharge, both dry and hanging-drop smears, disclosed many active forms of *E. histolytica*. The discharge was acid in reaction and presented a few pus cells, many eosinophils, red blood cells, and vaginal cells, with Gram-positive cocci and a few Gram-negative bacilli. Scrapings from the ulcers again revealed active *E. histolytica*. The discharge obtained by milking the urethra presented, both by dry and hanging-drop smears, active forms of *E. histolytica*. Biopsy of an ulcer showed evidence of subacute inflammation but no *E. histolytica*.

Examination of the stools revealed cysts of *E. histolytica*, but proctoscopy showed no ulcer in the lower anorectal canal. Other evidences of amoebiasis were the enlarged tender liver and slight tenderness and thickening of the descending and iliac colon. There were a few leucodermic patches in the region of the waist.

Treatment

Treatment with emetine hydrochloride was started. It was given in daily doses of 1 gr. (65 mg.) intramuscularly. The vagina was cleaned twice daily with warm normal saline douches. After five days the discharge and discomfort were much relieved and examination could be undertaken without anaesthesia. The ulcers were healed or healing. The cervical lesion looked smaller and the external os could be detected. The cervical discharge was aspirated and showed a few *E. histolytica* with very sluggish movement. They were almost round, and looked like the precystic forms of the parasite.

The patient was complaining of some vague hypogastric pain associated with frequent micturition. A catheter specimen showed a number of entamoebae again moving sluggishly. No local treatment was given for this amoebic trigonitis or cystitis. Treatment with emetine was continued, and "stovarsol" vaginal compound was given every night after the saline douches. She was also given an alkaline mixture.

After 12 gr. (0.8 g.) of emetine in fifteen days the ulcers were completely healed and the patient felt perfectly well. No urinary symptoms remained, and examination of urine and vaginal discharge revealed no abnormality.

Discussion

Three points favour the diagnosis of amoebic vaginitis: (1) Vegetative forms of *E. histolytica* in the discharges and scrapings from the ulcer. (2) Rapid cure with specific amoebicidal drugs. (3) The punched-out character of the ulcers, with slightly overhanging edges and sometimes yellowish bases, situated mostly in the furrows between the folds of the vaginal mucosa, which shows very little inflammatory reaction.

Infection of the vagina is presumably by continuity and contiguity with the anorectal canal, and this may be helped mechanically by the method of ablution practised in Bengal to cleanse the part after defaecation.

The cervix is involved in about 70% of the reported cases, and the ulcer is usually placed eccentrically and away from the external os. The uterus is often enlarged, and it may be that many or all of the cases in which the uterus is enlarged, soft, and tender have some infection of the uterus. Uterine aspiration was not done in any of the reported cases.

Leucorrhoea due to *E. histolytica* may be fairly common in India. Cases should be investigated thoroughly from this point of view.

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Medical Memoranda

Perforation of Stomach in Scrotal Hernia

Owing to the rarity of this condition (only one other case of this type occurs in the literature: Jayle, 1893) I feel that the following is worthy of record.

CASE REPORT

The patient, a man aged 66, was sent into hospital for ? strangulated left inguinal hernia. He had had a left inguinal hernia for 35 years. Two months previous to his admission he had undergone prostatectomy here, with an uneventful recovery. At the time it was noticed that he had a small left inguinal hernia; since the operation he had been perfectly well. Twenty-four hours before admission the hernia had descended into the scrotal sac, and one hour before admission the patient experienced a sudden severe pain over the left inguinal region, accompanied by nausea and vomiting, the vomitus being gastric contents. The pain was continuous; he was crying out in agony, and disliked being moved. His last bowel motion had been twelve hours before admission, and he had passed urine that day.

Examination showed a well-covered muscular man. His general condition was reasonably good, but he was dehydrated. Temperature 96.4° F. (35.8° C.); pulse 126; respirations 44. He had a large scrotal swelling 12.5 cm. in diameter, which filled the whole of the scrotum. The scrotum was tender, but not excessively so, and was resonant on percussion. The patient complained of severe pain and tenderness over the region of the external inguinal ring. There was some slight abdominal rigidity. Peristaltic sounds were heard and the abdomen was generally resonant. The tongue was furred and dry, and the lungs and heart were normal. A diagnosis of strangulated left inguinal hernia was made, and the patient was given ¼ gr. (16 mg.) of morphine, was put on a glucose-saline drip, and was prepared for the theatre.

Operation.—This was done by Mr. Ganz (anaesthetic: thiopentone, cyclopropane, and curare, administered by Dr. Waters). A T-shaped incision was made over the left inguinal region—the horizontal part of the incision parallel to the inguinal ligament and the vertical part over the scrotum. The coverings of the hernia were separated and the peritoneum was opened. Fragments of yellowish inspissated material and about 4 oz. (56 g.) of golden-coloured fluid were present in the scrotal sac. The bowel was delivered from the scrotum and found to consist of a portion of the stomach, some coils of small intestine, the transverse and pelvic colons, also the descending colon, which was provided with a mesentery. There were also small pieces of food in the scrotal sac. The bowel was returned to the abdominal cavity and the skin incision prolonged upwards; a large perforation 5 cm. by 5 cm. was found on the lesser curve of the stomach. The adjacent stomach wall was extremely thin. The perforation was sutured and oversewn with a double layer of stitches and an omental graft. The wound was closed and nylon skin sutures were inserted. On the return of the patient from the theatre he was given penicillin, sulphathiazole, and continuous oxygen, but his condition deteriorated and he died the following day.

Necropsy.—The abdomen was moderately distended. On opening the peritoneum a purulent acute generalized peritonitis was found, with much pus under the right lobe of the liver and in the right paracolic gutter. Inspissated yellowish-brown faecal-looking lumps of material were scattered all over the peritoneal cavity. A large hernial sac was occupied by loops of both small and large bowel and a number of similar lumps of material as mentioned above. The orifice of the sac was three fingerbreadths and was surrounded by a firm fibrous ring. The stomach was exceedingly mobile and elongated, with a scarcely definable lesser omentum. A piece of greater omentum was sutured over and partly closed a long oval hole (8 cm.) about the centre of the lesser curve. This perforation was through a blackened gangrenous area of stomach wall, and gastric contents had exuded into the peritoneal cavity and lesser sac. Obviously necrotic stomach wall extended 4 cm. around the perforation. There was no evidence of a chronic peptic ulcer. A few small thrombosed veins were present in the affected stomach wall, but no other vascular occlusion could be found. The right and left gastric arteries were normal. No pressure ring could be discerned to suggest the site of strangulation.

Examination of the C.V.S. failed to show any source of embolism. The pathologist's comment was: "It appears that this was a Richter's hernia in which the stomach was strangulated followed by perforation."

COMMENT

The probable course of events was that a portion of the large bowel had entered the hernial sac, this being rendered easy by its mobile mesentery; the stomach had been dragged into the sac by the gastrocolic omentum, and the lesser curve had been strangulated at the neck of the sac, with subsequent perforation of the stomach wall. Though the perforation was sealed at operation it is apparent that a further area of stomach wall had necrosed and subsequently perforated, resulting in the death of the patient.

My thanks are due to Mr. J. B. Marinan, medical superintendent, for his permission to publish this case and for his interest and helpful suggestions, and to Dr. J. Ennis for his post-mortem report.

H. SIMMONS, L.R.C.P., L.R.C.S.Ed.,
Late House-surgeon, Dryburn Hospital, Durham.

REFERENCE

Jayle (1893). *Bull. Soc. Anat. Paris*, **68**, 42.

A "Third Ureter" in Prostatectomy

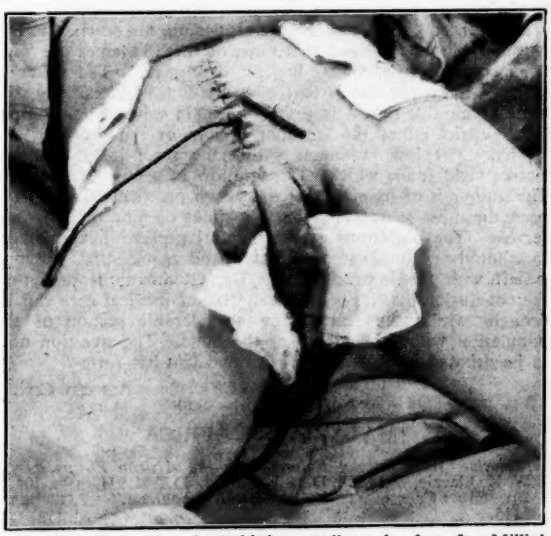
Despite the sanguine views of many of my surgical confrères regarding the control of haemorrhage in the various forms of prostatectomy with bladder closure, I am dissatisfied in this respect. While not unmindful of the wholesome effects of the closed bladder after prostatectomy, sisters and house-surgeons have come to regard it with no little concern and even apprehension because of reactionary bleeding and clots lodging in the urethral drain, with distressing results. One finishes the operation with a gratifying degree of haemostasis, yet a day or two later one too often meets with disquieting reports of catheter difficulties, and evidently the staff have been somewhat anxious and harassed. The patient shares in the agitation instead of resting quietly after his ordeal. For his comfort and safe healing, and for the contentment of the surgical team, something more is needed in post-operative technique.

Catheter drainage depends on two factors—paucity of blood and plenitude of urine delivered by the ureters. Unfortunately, owing to the shock of operation and the subnormal intake of fluids, the kidney action is all too often in abeyance. Accordingly I have tackled the problem from this direction. Since we cannot rely on adequate repression of bleeding, the logical remedy is to compensate for surgical oliguria by artificial "diuresis," using a rubber tube drip of dilute antiseptic from a bedside reservoir. This "third ureter" pleases everyone, including the patient, who prefers an automaton to intermittent service by nurses punctuating his repose for a day or so after operation and sometimes resorting to regrettably forceful syringing and sucking to clear his clogged drain.

The technique is not intended to cover slackness in surgical haemostasis but to confer on residents and nurses a feeling of calm confidence instead of anxiety that taxes their energies unduly during aftercare. I use the procedure after all three operations (Harris, Hey, or Millin), and even after resectoscopy occasionally insert a small suprapubic drain. As "third ureter" I employ a Jacques (No. 4) catheter, the orifice of which rests on the base of the bladder.

METHOD

A small Lister bougie is introduced (via the bladder-neck in Millin's operation) and pressed up against the dome of the bladder, which is incised for the tip to protrude. On this I slide the catheter by its open end after having cut off the tip. The sound is withdrawn with the catheter into the bladder and then detached. A stitch tethers the catheter to the skin, and anchorage is reinforced by "elastoplast" to prevent its being dragged out by inadvertent pulls. A glass connexion joins the outer end with light rubber tubing, which is interrupted by a glass drip on its way to a douche-can of irrigating fluid on a stand by the patient's bedside. The urethral catheter (24E) draining the bladder is suspended by a single nylon thread which pierces the bladder and abdominal walls about 1 in. (2.5 cm.) from the midline and is tied to a Harris metal rod. The outer end of this urethral drain is joined to a rubber tube of about the same calibre and not too readily compressible (see Figure), which ends a foot from the bottom of the bucket. Irrigation is set going at about 50 drops a minute for the first few hours, and the speed is adjusted by a screw-clamp to the safe degree of dilution. To dispel doubts arising about a clear channel, release the clamp and flush through the system.



Photograph showing the "third ureter" on the day after Millin's prostatectomy.

The constancy of the irrigation is assured not only by the staff's seeing the issuing drip, but the patient or the nurse, even in the dark, can also tell by the friendly sound of the drops. This continues for about 48 hours, by which time the water is generally a pale red hue or clear. The vital injunction to the nurse is, "Never leave the drip running in unless there is a corresponding outflow." The procedure can continue with the patient sitting out of bed, or it may be interrupted while he moves about. The "third ureter" is removed on the third or fourth day. Subsequent leakage is absent or negligible.

A. WILFRID ADAMS, M.S.

Reviews

STATE MEDICINE IN THE U.S.A.

Voluntary Medical Care Insurance in the United States. By Franz Goldmann, M.D. (Pp. 228. 16s.) New York: Columbia University Press. London: Geoffrey Cumberlege. 1948.

All the signs point to the early provision of some form of national health insurance in the U.S.A. There is a voluminous literature on the subject, and Dr. Goldmann has added to it a useful objective examination of how far voluntary schemes have provided, or failed to provide, medical care for the community. Every writer on the topic agrees that the usual system of payment per service rendered fails to meet the needs and financial capacity of a considerable section of the community. The organized medical profession, while admitting this, has claimed that the problem would be manageable by a voluntary system of prepayment.

This book shows that efforts to achieve such a solution have been numerous. Some have been sponsored by commercial insurance companies, some by combinations of employers and employees, some by organized groups of doctors. The majority of the schemes provide only for hospital cases. At the end of 1946 over twenty-four million persons were enrolled in hospital service schemes, as against some five million in schemes providing home and general treatment. Dr. Goldmann says that many practitioners view with apprehension the popularity of the hospital schemes, which could, and sometimes do, favour practice from as well as in the hospitals. The author comes to the conclusion that so far as plans for general medical care are concerned "the lower income groups are not reached to any considerable extent," and that most of these schemes are "far from comprehensive in the benefits they offer." The difficulty with all these projects is that of attracting, and retaining, the more favourable risks. In order to remain solvent the sponsors must restrict either the freedom to join or the scope of the service. The low premiums within the reach of the poorer classes yield funds which will not allow of a complete service. The author is of opinion that the group practice schemes have been the most successful from the point of view of scope of service. The objections of the medical profession and others to compulsory insurance are stated and appreciated, but one is left with the impression that Dr. Goldmann is driven to the conclusion that no complete system of medical care can be brought within the reach of a considerable section of the population without the help of the State. The question now to be debated is, How much help, and in what form?

ALFRED COX.

MALARIA IN AFRICA

Malaria. With Special Reference to the African Forms. By W. K. Blackie, M.D., Ph.D., F.R.C.P.Ed., D.T.M.&H. (Pp. 104. 10s. 6d.) Capetown: "The African Bookman." P.O. Box 3115.

Malaria Control by Coastal Swamp Drainage in West Africa. By A. B. Gilroy, O.B.E., M.B., B.S.(Melb.), D.T.M.&H.(Eng.). (Pp. 97; 22 plates. No price.) London: Ross Institute of Tropical Medicine.

If in the past Africa has had a reputation for backwardness this should not apply to the future. For if Africa could be ridded, as now seems possible, of malaria and tsetse fly it promises to play in the future a large part in the economic affairs of the world. These two small books are indicative of the interest now taken in Africa in the control of the first of these adverse conditions. Dr. Blackie gives a good short description of malaria. It is likely to be useful to the practising medical man as providing an up-to-date account of modern antimalarial treatment; though the reviewer would have thought it better to refer to the intramuscular administration of quinine only as a form of treatment that need never now be used, since, if intramuscular injection must be given, mepacrine is preferable.

The second work is more unusual. Dr. Gilroy gives an account of malaria control operations carried out since 1942 at Lagos. Lagos is a town originally crowded on to a small sandy estuarine island, but with its increasing population and importance it has lately extended on to the only land available—low-lying tidal swamp, much of it mangrove. Fortunately recent research on malaria under these conditions has been helpful, and the study of the mangrove and of the special habits of the species of anopheles concerned in transmission has given a clear indication of the kind of measures to be adopted. The description given of the natural history of the different kinds of mangrove, the kinds of swamp they give rise to, and the relation of these to the tides and the breeding places of anopheles makes interesting reading, as also do the very clear accounts of the different operations undertaken. The book is enlivened with some clever sketches of operations in progress and with photographs giving the different types of swamp and the nature of the engineering work carried out.

S. R. CHRISTOPHERS.

PRACTICAL GUIDE TO LEPROSY

Manual of Leprosy. By Ernest Muir, C.M.G., C.I.E., M.D., F.R.C.S.Ed. (Pp. 208; 70 illustrations, several in colour. 17s. 6d.) Edinburgh: E. and S. Livingstone. 1948.

This small book has been written for the guidance of doctors, nurses, and lay workers who undertake leprosy work. For this reason the author discusses mainly clinical features, treatment, and the methods of prevention in common use, and devotes little space to history, prevalence, and epidemiology. His account of the histology and the reaction of the tissues to the infection is good and illustrated by sections—some in colour—showing the tissue changes and the causative bacilli. He has adopted the recent South American classification based on histological changes instead of the clinical one of the Cairo Conference. The former is the more scientific, but it will prove to be rather confusing to the large proportion of field workers who have neither time nor facilities for making such examinations.

The clinical chapters are the most detailed and useful part of the book, and they are illustrated by photographs taken by the author. He records the treatment that he has long used, but omits to mention some preparations that other authorities have given with advantage. Dr. Muir advises injections of hydnocarpic oil intradermally and into the deeper tissues; he also mentions the use of the ethyl esters, which are generally relied on by American workers but are more expensive. He differs from some authorities in recommending intermissions in the courses of injections. He advises sulphone treatment in lepromatous cases and also suggests that it be tried in the "uncharacteristic" type with negative lepromin reactions. Recent trials of sulphetrone indicate that it is less toxic than other forms, but it is still too early to decide on the precise value of this new line of treatment. The concluding section of the book is a practical account of the methods now in general use for the control of leprosy. He advocates compulsory segregation in endemic areas when accommodation is available, and also discusses home isolation. He recommends the examination of school-children and gives much good advice. This book embodies great practical experience and will be of value to those for whom it is intended.

LEONARD ROGERS.

ESSAYS IN PSYCHIATRY

The Yearbook of Psychoanalysis. Edited by S. Lorand, M.D., and others. Volume 3, 1947. (Pp. 308. £1 10s.) London: Imago Publishing Company. 1948.

The third volume of this series maintains the standards set by the first two. It is to be regretted that the publishers persist in describing it as a compendium of recent advances in the theory and practice of psycho-analysis. Although it contains few research contributions of value, it is certainly an interesting collection of essays on a wide range of subjects from a correlation of the basic ideas common to Freud and to Spinoza (Bernard, New York) to such curious matters as the charming away of sties by means of barley and wedding-ring rituals (Inman, London). Of the clinical papers the most outstanding are those by Garma (Buenos Aires) and by Jacobson (New York) on various aspects of melancholia and on the effect of disappointment on depressive development,

and one by Schonberger (Budapest) on the nightmare syndrome. A summary by W. C. Menninger (Topeka) of modern concepts of war neurosis is notable mainly as demonstrating the absence of any significant advances in this field despite the opportunities afforded by the second world war.

Although yearbooks of this sort usually demand considerable technical understanding on the part of the reader, this particular issue contains a number of papers of more general interest, in particular Ernest Jones's valedictory address and E. D. Adrian's lecture on the mental and physical origins of behaviour. A number of articles on applied psycho-analysis by, among others, Wittels (New York), Marie Bonaparte (Paris), and the late Hanns Sachs provide additional attractions for the non-analytical reader.

Excellent as it is, the volume would have been greatly improved by the omission of several rather platitudinous short articles and of a longish but very superficial and unilluminating study on the anti-Semitic character.

EDWARD GLOVER.

MENTAL DEFICIENCY

A Textbook of Mental Deficiency (Amentia). By A. F. Tredgold, M.D., F.R.C.P., F.R.S.Ed. Seventh edition. (Pp. 534; 47 plates. 30s.) London: Baillière, Tindall and Cox. 1947.

For forty years Dr. Tredgold's scholarly textbook on mental deficiency has held a unique position. A medical subject which has tended to be neglected in the writings of neurological and paediatric specialists receives attention here in a manner particularly well adapted to the needs of both clinicians and administrators. In the new edition the original illustrations—many of them wisely chosen from Dr. Brushfield's and Dr. Turner's case photographs—have been supplemented by other excellent pictures. New features include notes on amentia due to Rh incompatibility and on the Laurence–Moon–Biedl and Rud syndromes, but the discussions on prenatal infections have not been expanded. The author provides copious information on legal and administrative problems and has brought it up to date by including an account of the effects of the Education Act of 1944.

Readers will be glad to find that the attractive discussions on isolation amentia and idiot savants still hold their places in the book. The only disappointment is that the classification of the clinical varieties of amentia summarized on p. 65 is substantially unaltered. The grouping is not easy to justify in the light of modern genetical thinking, though it is admittedly difficult to find any really logical method of classification. Dr. Tredgold's lucid style of writing makes the book a pleasure to read. This is most fortunate in a textbook which it is essential for all serious students of the subject to master, whether or not they agree with all the views expressed.

L. S. PENROSE.

HOSPITAL MANAGEMENT

On Hospitals. By S. S. Goldwater, M.D. (Pp. 395; illustrated. $9.00 or 45s.) New York and London: The Macmillan Company. 1947

Dr. S. S. Goldwater, who died in 1942, had a distinguished career as a health-service and hospital administrator, having been Superintendent and Director of the Mount Sinai Hospital, New York, Commissioner of Health of the City of New York, and Consultant in Hospital Organizations and Planning. This book is a collection of the essays, papers, and reports written by him during his long career, together with plans of many of the hospitals for which he was responsible.

He discusses the whole range of hospital management and construction, and every word is inspired by his obvious devotion to the cause he had at heart. Most of his ideas were far ahead of his time, but very few have not now been accepted: those concerned with the social aspects of hospital administration are cases in point, and most of them are now implicit in all our thinking. While many of the essays are lucid expositions of the whole philosophy underlying provision of care for the sick, the author never loses sight of the material aspects. His influence on the development of community health care and on the planning of hospitals was probably greater than that of any other man of his time.

ANDREW TOPPING.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

New and Nonofficial Remedies, 1948. (Pp. 800. 21s.) London: J. B. Lippincott. 1948.

Issued by the Council on Pharmacy and Chemistry of the American Medical Association.

Pediatrics and the Emotional Needs of the Child. Edited by H. L. Witmer. (Pp. 180. 8s. 6d.) London: Geoffrey Cumberlege. 1948.

Papers read at a joint discussion by American paediatricians and psychiatrists.

The Biology of Bacteria. By A. T. Henrici, M.D. 3rd ed. (Pp. 577. 25s.) London: George G. Harrap. 1948.

An introduction to general microbiology.

The Management of Binocular Imbalance. By E. Krimsky, M.D. (Pp. 464. 63s.) London: Henry Kimpton. 1948.

From the New York Polyclinic Medical School.

Primary Anatomy. By H. A. Cates, M.B. (Pp. 478. 33s.) London: Baillière, Tindall and Cox. 1948.

For nurses, physiotherapists, and others of similar interests.

Psychiatry. By H. C. Beccle, M.B., M.R.C.P., D.P.M. (Pp. 245. 17s. 6d.) London: Faber and Faber. 1949.

Theory and practice for nurses and students.

Surgical Pathology. By P. A. Herbut, M.D. (Pp. 710. 60s.) London: Henry Kimpton. 1948.

A new American work.

The Plant Alkaloids. By T. A. Henry, D.Sc. 4th ed. (Pp. 804. 63s.) London: J. and A. Churchill. 1949.

The new edition is largely rewritten.

Kayne, Pagel, and O'Shaughnessy's Pulmonary Tuberculosis. Revised by W. Pagel, M.D., and others. 2nd ed. (Pp. 720. 63s.) London: Geoffrey Cumberlege. 1948.

An extensively revised edition.

The Third Mental Measurements Yearbook. Edited by O. K. Buros. (Pp. 1,246. $12.50.) New Brunswick: Rutgers University Press. 1949.

A guide to recent work.

Penicillin and Other Antibiotics. By G. W. S. Andrews, M.B., B.S., and J. Miller, B.Sc (Pp. 160. 7s. 6d.) London: Todd Publishing Group. 1949.

A short survey of antibiotics.

Science in Liberated Europe. By J. G. Crowther (Pp. 336. 18s.) London: Pilot Press. 1949.

An account of the activities of European scientists before and after liberation.

Medical and Nursing Dictionary and Encyclopaedia. By E. Pearce. 9th ed. (Pp. 723. 17s. 6d.) London: Faber and Faber. 1949.

A further edition of the well-known dictionary for nurses.

Polio and its Problems. By R. H. Berg. (Pp. 174. 18s.) London: J. B. Lippincott. 1948.

A popular account of poliomyelitis.

Widening Horizons in Medical Education. A Report of the Joint Committee of the Associated American Medical Colleges and the American Association of Medical Social Workers. (Pp. 228. 15s.) London: Geoffrey Cumberlege. 1948.

A study of the teaching of social and environmental factors in medicine.

The Situation in Biological Science. (Pp. 631. 9s. 6d.) London: Collet's Holdings. 1949.

Proceedings of the Lenin Academy of Agricultural Sciences of the U.S.S.R., 1948.

BRITISH MEDICAL JOURNAL

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SATURDAY MAY 7 1949

A NEW TREATMENT FOR RHEUMATOID ARTHRITIS

Rheumatoid arthritis is known to have existed in prehistoric times, and the search for a cure has presumably continued ever since. In the course of time much information has accumulated about the natural history, pathology, and the provocative factors of the disease, but since the waning of belief in an all-important infective factor little certain information exists about its aetiology. In his recent Oration before the Heberden Society in London, Dr. P. S. Hench[1] reiterated the known facts and pointed out that rheumatoid arthritis has two sharply contrasting characteristics—that of potential chronicity and that of potential reversibility. He divided the causes of reversibility into spontaneous, therapeutic, and accidental. Spontaneous remissions have always been recognized as a possible occurrence even in cases in which the prognosis seems hopeless[2]; therapeutic remissions can be induced in a proportion of cases by means of gold therapy or blood transfusion; whilst accidental remission may frequently occur in pregnancy and in jaundice of certain types.

Consideration of these facts makes it increasingly difficult to harmonize the microbic theory of the origin of rheumatoid arthritis with modern knowledge. It seems more probable that the disease is part of a basal biochemical disturbance of unknown type which is accidentally and transiently corrected by some biological change common to a number of apparently unrelated conditions—pregnancy and jaundice being the most notable. Hoping to reproduce the beneficial effects of pregnancy, physicians have administered fairly large doses of female hormones to non-pregnant sufferers from rheumatoid arthritis, but the results have mostly proved to be disappointing, as has the employment of transfusions of blood from pregnant women—a form of therapy which was recently advocated.[3]

Last year workers at the Mayo Clinic put forward the conjecture that the anti-rheumatic factor might prove to be one of the adrenal hormones. Recent work by Selye[4,5] and others on the biochemical changes induced in animals exposed to a wide variety of noxious agents has shown that the changes vary with the intensity and the duration of the stress but are independent of its nature. This has been termed the "general adaptation syndrome," and has been shown to be due to excessive secretion by the anterior pituitary gland of corticotropin, which in turn stimulates increased adrenocortical secretion. Continued application of the stress is accompanied by continued hyperactivity of the hypophysio-adrenal mechanism, and for a time there is high resistance to the particular agent used and increased susceptibility to all others. Ultimately all resistance breaks down when the adaptive energy is exhausted.

Interest in this syndrome was aroused when Selye pointed out that it lent itself to a concept of "adaptation diseases." By various experimental procedures he produced in animals changes in the joints and the heart similar to those observed in human rheumatism, and concluded that "the adrenal cortex may play an important role in the pathogenesis of rheumatic and rheumatoid conditions in man."[6] Further experiments have shown that the essential requirement to enable these and other pathological changes to be brought about is an excess of salt-active corticoid hormone. This would suggest that during the phase of resistance the increased corticoids, which are normally beneficial, are capable in certain circumstances of producing recognized disease syndromes. Knowlton,[7] searching for the modifying factors which in most cases presumably prevent the effect of stress resulting in "adaptation" disease, suggest that such disease is the result of a dual mechanism—the one factor being the non-specific effect of corticoids and the other a property specific for the given stress and the determinant of the site of the effect.

In September, 1948, Kendall was able to provide for Hench and his colleagues at the Mayo Clinic a supply of 17-hydroxy-11-dehydrocorticosterone (compound E) for clinical trial.[8] This was administered to a female patient, aged 29, who had had severe rheumatoid arthritis for 4½ years. She had not responded satisfactorily to any method of treatment, and many joints were swollen, stiff, and very painful on any movement. Radiographs disclosed severe destructive changes in her right hip and less severe lesions in other joints. The blood sedimentation rate was 108 mm. (Westergren), and the patient's condition appeared to be deteriorating. On Sept. 20, 1948, she could hardly get out of bed, and on that day intramuscular injections of compound E were started in daily doses of 100 mg. No change was noted until Sept. 30, when she rolled over in bed for the first time with ease and reported much less muscular stiffness and pain. On the next morning all muscular stiffness had left her, her appetite returned, and she was able to walk with only a slight limp. By the seventh day of treatment all tenderness and pain on movement and even swellings were greatly lessened. The next day she went out shopping for three hours, returning tired but with no stiffness or pain. The progress made by this patient was for various reasons not fully maintained, but since then a total of 14 other cases have been treated, in all of which considerable and rapid improvement has been noted. Since January, 1949, compound E acetate, a more easily prepared and less expensive product, has been used in place of compound E, with equally good results.

Two female patients with severe rheumatoid arthritis were also treated with 100 mg. of pituitary adrenocorticotropic hormone (ACTH) intramuscularly for 12 days. The results of metabolic studies on these patients have yet to be published, but it is reported that clinical improvement

[1] *Ann. rheum. Dis.*, 1949, in the press.
[2] Davidson, L. S. P., in Copeman, W. S. C., *Textbook of the Rheumatic Diseases*, 1948. Edinburgh.
[3] Barsi, I., *British Medical Journal*, 1947, **2**, 252.
[4] *J. clin. Endocrinol.*, 1946, **6**, 117.
[5] *Ann. intern. Med.*, 1948, **29**, 403.
[6] *J. Amer. med. Ass.*, 1944, **124**, 201.
[7] *Endocrinology*, 1946, **38**, 315.
[8] *Proc. Mayo Clin.*, 1949, **24**, 181.

similar to that resulting from the use of compound E occurred promptly in both.

The number of patients so far treated by this new method is small. This is due principally to shortage of supplies of the hormone; great efforts have been made to overcome this, but the technique of preparation is difficult, time-consuming, and expensive. As a control experiment the injections of compound E were at times, unknown both to the patient and the administrator, replaced by an inactive solution. When this was done articular and muscular symptoms recurred within a few days, and the sedimentation rate rose in every case. No serious toxic reactions have been noted as the result of administration of compound E or its acetate, with the exception of transient oedema. Nevertheless much more experience is needed before sufficient knowledge will be acquired about its efficacy and safety with prolonged administration.

The effects of related compounds such as dehydrocorticosterone (compound A), 17-hydroxycorticosterone (compound F), desoxycorticosterone (DCA), and pituitary adrenocorticotropic hormone (ACTH) are being investigated by Hench and his colleagues. Some years prior to the recent war a small-scale trial of the effect of desoxycorticosterone on rheumatoid arthritis was carried out by the Empire Rheumatism Council in this country, with negative results, but, so far as is known, none of the other compounds mentioned have yet been applied to the treatment of the rheumatic group of diseases.

It would appear from the information so far available that a therapeutic discovery of the greatest importance has been made. It is of course unfortunate that the amounts available of both compound E and of the adrenocorticotropic hormone are so small, and are likely to remain so until these substances can be synthesized. However, arrangements are in hand for a thorough trial in this country when supplies are adequate.

ESSENTIAL HYPERTENSION

Since Sir Clifford Allbutt[1] first recognized 50 years ago that arterial hypertension sometimes arises in the absence of renal disease research into what is now called essential hypertension has gained such impetus, especially during the last decade, that it has become a difficult task for the clinician to keep in touch with the rapid advances being made, and still more difficult for him to correlate their significance. Clamping of the renal arteries in animals seems far removed from non-renal hypertension in man, and the recognized influence of heredity is at first glance a paradox, since there is a growing impression, recently referred to in this *Journal* by Ogilvie,[2] that hypertension is a stress disease. It is not even clear whether it is a single disease or a symptom complex. The lectures given by Professor F. H. Smirk at the British Postgraduate Medical School and reported elsewhere in this issue of the *Journal* are therefore welcome, since they help to put the many current problems of essential hypertension in clear perspective.

[1] *Abstr. Trans. Hunterian Soc.*, 1895–96, 38.
[2] *British Medical Journal*, 1949, **1**, 645.
[3] *Studies of the Renal Circulation*, 1947, Oxford.
[4] *Quart. J. Med.*, 1947, **16**, 111.
[5] *Hypertension and Nephritis*, 1939, Philadelphia.

It is generally accepted that the raised blood pressure in essential hypertension frequently precedes pathological changes in the arterioles, and that sustained hypertension causes or accelerates the development of arteriosclerosis. It follows that renal ischaemia due to vascular changes cannot be the initial factor in the production of essential hypertension in young subjects. In later life, however, pathological changes in the renal arterioles are always present. Essential hypertension arising after the age of 45 may possibly be secondary to these changes, and it is conceivable that the disease in youth is aetiologically distinct from that arising after middle age. It is fundamental to the understanding of essential hypertension to realize that an increase in the blood pressure due to any cause, physiological or pathological, may be followed by a further increase, this secondary hypertension often persisting after the primary cause has ceased to operate. The mechanism by which the secondary rise in blood pressure is brought about is not clearly understood. Arteriosclerotic changes in the large vessels are not the cause, for they increase only the systolic pressure; and Volhard's theory that pathological narrowing of the arterioles causes increased peripheral resistance has now been disproved. It is known that ischaemic kidneys liberate renin, a pepsin-like enzyme; this is activated by a substrate (pre-angiotonin) found in normal serum to form a polypeptide, angiotonin, which causes vasoconstriction. Thus any stimulus producing vasoconstriction, and therefore renal ischaemia, will lead to angiotonin formation, further vasoconstriction, and an additional rise in the blood pressure.

The stimuli capable of starting this vicious circle may be functional rather than pathological, and the possible role of the renal shunt demonstrated by Trueta and others[3] is plain. Another important factor is that the enlarged arterioles in hypertension respond excessively to vasoconstricting stimuli, so that once medial hypertrophy has taken place vasoconstriction is more readily maintained. The relative importance of these two factors is difficult to assess, but the variable response of different experimental animals subjected to the Goldblatt clamp serves as a warning against the unreserved acceptance of this mechanism in man. The persistence of hypertension after the cessation of the primary stimulus is usually attributed to renal arteriosclerosis, which develops during the period of primary hypertension. However, a non-renal mechanism is also possible, as shown by the persistent raised blood pressure in rats after bilateral nephrectomy.

Though the exact nature of these complicated mechanisms may not be clear, the implications are plain: any stimulus producing vasoconstriction will in time lead to permanent hypertension, and essential hypertension may arise either from exposure to excessive stimulation or from exaggerated vascular response to normal stimuli. The basic causes of hypertension are therefore to be sought in undue stress or in individual diathesis. The hypertensive diathesis can often be demonstrated clinically by an abnormal rise in the blood pressure following immersion of the arm in ice-cold water—subjects showing a positive response to this test being more liable to develop hypertension than those who respond normally. It is well known that the incidence of essential hypertension is higher

in some races than in others, and Platt[4] has recently shown that hypertension is largely a hereditary disease, being transmitted as a Mendelian dominant. But stress factors are equally important; for example, African negroes lose their immunity to hypertension when living in the environment of Western civilization. The link between obesity and hypertension is not purely genetic: the obese hypertensive patient may become thin and normotensive through dieting alone—a fact sometimes overlooked in the treatment of the obese middle-aged patient with hypertension. Response of the blood pressure to emotion and mental effort varies greatly, but it has been shown that those who react to such stimuli with the greatest rises of blood pressure are more liable than others to develop permanent hypertension in later years.

Malignant hypertension is regarded by most authorities as a form of essential hypertension with a great increase of the diastolic pressure and acute arteriolar necrosis, and Fishberg[5] prefers to call it the malignant phase of essential hypertension. Professor Smirk does not accept this concept as proved. He points out that malignant hypertension is rare in the province of Otago, New Zealand, and so also is chronic glomerulonephritis. He suggests that the two diseases may have some aetiological factor in common. Whatever may be the outcome of further studies on this possible relationship, the suggestion is in keeping with the theme of Professor Smirk's hypothesis: essential hypertension is not a single disease but a clinical state arising as the end-result of numerous primary causes. The cause may be physiological, as in environmental or emotional stress, or pathological, as in renal and endocrine disorders. The disease perhaps arises for different reasons in old age and in youth, and it may well be that malignant hypertension has a different primary cause. This wider concept of the disease should lead to further investigations of the factors in everyday life which are responsible for essential hypertension ranking so high in the diseases of civilization.

STILBOESTROL THERAPY IN PREGNANCY

Another contribution to the study of gynaecological and obstetrical endocrinology comes from O. W. Smith,[1] who now describes the results of four years' clinical and laboratory research on the action of diethylstilboestrol in pregnancy. Having persuaded clinicians in various parts of the U.S.A. to join in the work she is in a position to assess the value of giving stilboestrol as a routine from the results obtained in 632 pregnancies. The theoretical basis of the investigation lies in the claim by O. W. Smith and G. V. Smith[2] to have shown that oestrogens increase production of progesterone in non-pregnant women by stimulating the pituitary and in pregnant women by bringing about better "utilization of chorionic gonadotropin." In this respect diethylstilboestrol is held to be superior to the naturally occurring oestrogens because its action is not depressed by progesterone already in circulation. O. W. Smith postulated that stilboestrol should be beneficial in pregnancy not by virtue of its own oestrogenic properties but by stimulating the placenta to secrete both oestrogen and progesterone. She therefore administered stilboestrol in cases of threatened and habitual abortion in "physiological" dosage, calculated according to the period of gestation. The results were good. Of 127 patients who had had at least two previous consecutive abortions, 102 (80%) were still pregnant after 28 weeks and 98 (77%) bore living babies, while of 38 women who had had three successive abortions 33 produced living children.

These are higher figures than the rates for spontaneous cure calculated by Malpas[3] and Eastman[4] in similar series of cases. Moreover, there was no evidence that the hormone treatment of threatened and habitual abortion increased the incidence of viable malformed foetuses. Vaux and Rakoff[5] had previously reported good results with combined oestrogen and progesterone therapy in habitual abortion, as also had White[6] in pregnant diabetic women. These writers regarded their form of treatment as substitution therapy, whereas Smith looked upon hers as stimulative—which should give better results, since the secreted hormones are likely to be supplied at a more uniform rate and in closer conformity to physiological needs. Many of Smith's patients received small daily doses of stilboestrol during the cycle of conception in order to improve luteal secretion and thereby provide a more thorough preparation of the endometrium for the fertilized ovum. This theory might therefore be used to explain the successful results recently reported in this *Journal* by Christie Brown,[7] who treated sterility and abortion with small doses of dienoestrol and progesterone, though according to Smith the progesterone is unnecessary.

Since the Smiths had claimed[2] that the toxaemias of late pregnancy are invariably preceded by a state of oestrogen and progesterone deficiency, it was natural that they should also inquire into the value of stilboestrol in the prevention of these conditions. They argue that it is unlikely to cure established toxaemia, because by the time signs appear syncytial degeneration and placental vascular damage are already present and the placenta is incapable of increasing its hormone production even under an extra stimulus. Encouraging results were obtained in the prophylactic treatment of 95 patients, only 18 of whose previous 197 pregnancies had been normal. Late pregnancy toxaemia and premature labour are relatively common in women with essential hypertension, yet in 17 hypertensive patients a 42% foetal loss sustained in previous pregnancies was reduced to 12% with this treatment. Again, 11 pregnant diabetic women, whose 13 previous pregnancies had resulted in only two living babies, produced eight living children following routine stilboestrol therapy, and none of them developed toxaemia. Three of the babies were large, which tends to support the statement by Barns[8] in a paper recently published in this *Journal* that there is no apparent connexion between the large size of babies of diabetic mothers and the presence of hormone imbalance or toxaemia in the mother.

The complicated theoretical basis of Smith's work may not meet with general acceptance. For instance, there is little evidence as yet to support the idea that the production of hormones by the placenta is under endocrine control. Again, other workers[9] have failed to find that a fall in oestrogen and progesterone output invariably precedes the development of toxaemia. Furthermore Davis and Fugo[10] gave stilboestrol to ten pregnant women and found no increase in pregnanediol excretion, though after the administration of progesterone this was increased. Their cases, however, were normal pregnancies, while Smith's original

[1] *Amer. J. Obstet. Gynec.*, 1948, **56**, 821.
[2] Smith, O. W., Smith, G. V. S., and Schiller, S., *J. clin. Endocrinol.*, 1941, **1**, 461.
[3] *J. Obstet. Gynaec. Brit. Emp.*, 1938, **45**, 932.
[4] *Progress in Gynaecology*, 1946, p. 262. London.
[5] *Amer. J. Obstet. Gynec.*, 1945, **50**, 353.
[6] *Penn. med. J.*, 1947, **50**, 705.
[7] *British Medical Journal*, 1948, **2**, 851.
[8] Ibid., 1949, **1**, 51.
[9] Taylor, H. C., and Scadron, E. N., *Amer. J. Obstet. Gynec.*, 1939, **37**, 963.
[10] *Proc. Soc. exp. Biol.*, 1947, **65**, 283.
[11] Smith, O. W., Smith, G. V. S., and Hurwitz, D., *Amer. J. Obstet. Gynec.*, 1946, **51**, 411.

work[11] was carried out on pregnant diabetic women; and their dosage of stilboestrol was considered by Smith to be so excessive that it might depress rather than enhance placental function. It could also be argued that the general care and close supervision which inevitably accompany any special therapeutic trial might in part explain the good results. Indeed, all manner of theoretical and practical questions arise, but the latter at least might be settled by observing the results of giving stilboestrol as a routine during pregnancy in further large-scale, carefully controlled clinical experiments.

GONORRHOEA IN WAR

The management of gonorrhoea in the second world war was very different from that in the first. The sulphonamides, which became available in 1937, and penicillin, which was first used in the treatment of gonorrhoea about May, 1943, completely changed the outlook. Whereas in the first world war enormous numbers of patients languished in large hospitals for weeks or even months, in the second a few days in hospital was the rule, and many Service patients were not even admitted to hospital but, particularly in the U.S. Forces, were treated on a "duty status." The incidence of complications fell from 28% in 1937 to less than 1% in 1944, and after the introduction of sulphonamide therapy the proportion of "carriers" decreased from between 5–20% to negligible figures. The progress made in World War II has been described by Altshuler,[1] who explains what lay behind the various orders issued for the management of gonorrhoea in the U.S. Army. The first of the sulphonamides to be used for this purpose was sulphanilamide, and this was succeeded in turn by sulphapyridine, sulphathiazole, and sulphadiazine. In 1941 the usual course of treatment was 19 g. of sulphathiazole in nine days, but it soon became apparent that 20 g. in five days gave better results, being successful in something like 75% of cases. When the first course failed a second similar one was given after five days, and in 1943 this second course was increased to 33 g. in five days. About this time sulphonamide resistance became a serious problem, with increasing numbers of patients failing to react. Many hospital beds were blocked, and morale suffered considerably. Almost the only effective treatment in such cases was hyperpyrexia; this meant maintaining the patient's rectal temperature at 105.8° F. (41° C.)–106.2° F. (41.2° C.) for eight hours—a procedure requiring much labour and skill, and by no means without risk.

Early in 1943 penicillin was found to be very effective against the gonococcus, and by June in that year 1,600 patients had been successfully treated on various dosage schedules. At first 10,000 units of penicillin were given every three hours for five doses, and if this failed 10,000 units were injected every hour for ten hours. These schedules were modified from time to time. One retained for a long period was 100,000 units in 15 hours. Later this was increased to 200,000 units, with correspondingly larger total doses in cases of relapse. Towards the end of 1945 there were indications that the gonococcus was developing some slight degree of penicillin resistance, and it was feared that the sulphonamide experience would be repeated. However, no well-authenticated case has yet been recorded, and most of the supposed cases have been due to faulty technique, insufficient dosage, or relatively inactive preparations of the drug. Relapse and development of the carrier state both proved to be much less common after penicillin than after sulphonamide therapy. In order to save the trouble of repeated injections various methods of prolonging the action of penicillin in the body by delaying absorption or excretion were investigated. Penicillin in peanut oil and beeswax proved effective and popular, though the viscidity of the preparation is troublesome; recently procaine penicillin in oil has come into use. With this preparation penicillin in the blood can be maintained at an effective level for 24 hours or so. At room temperature the solution will pass easily through an ordinary intramuscular needle. The use of penicillin made practicable the out-patient treatment of Servicemen suffering from gonorrhoea, and in the U.S. Forces this became the rule in 1945, though in the British Army the patient was normally seen by a specialist venereologist and "detained" for 24 to 48 hours—a more economic procedure than admission to hospital. Diagnosis in the Services has always presented a problem, since the normal "medical inspection room" or other centre to which a Service man ordinarily reports sick contains no facilities for smear or culture work, and a diagnosis of gonorrhoea is never justified (either in the U.S. or British Forces) on clinical grounds only. In the male a smear alone is usually sufficient, but in the female a culture is frequently necessary as well, particularly in subacute or chronic cases. However, the great majority of Service women suspected to be suffering from gonorrhoea were admitted to hospital for examination and treatment.

Criteria of cure were more exacting in the British than in the U.S. Forces. In the former three months' observation, with periodical clinical and pathological examinations, was the rule for both sexes; in the latter, three weeks' observation for men and three months' for women were considered adequate. One reason for this discrepancy was the much freer availability in the American Forces of penicillin, which was provided for the treatment of gonorrhoea in the latter long before similar provision was made for the British. The remaining problem was to determine the necessary period of observation in order not to miss a concurrently acquired syphilitic infection in patients who developed gonorrhoea and were treated with penicillin: opinions differ about how long this should be, but most authorities consider the period should be four months at least, and preferably six, while some put it at twelve. There can be no doubt that the treatment of gonorrhoea was one of the great medical triumphs of the war. Penicillin reduced what was a very serious medical problem to negligible proportions, and if it did not appreciably reduce the incidence of the disease it must have saved many thousands of hospital days, and thus much expense and manpower.

MUSCLE BIOPSY IN RHEUMATOID ARTHRITIS

The comprehensive term "rheumatism" has long been recognized to include a variety of conditions of different aetiology, and any unification that may be attempted in future must depend on something more than the common factor of pains in the limbs. One promising method of investigating the rheumatism problem was evolved by Curtis and Pollard[1] in America. They obtained from patients with rheumatoid arthritis pieces of skin and calf muscle in parts remote from the affected joints; these biopsies showed the presence of small foci of round cells of chronic inflammatory type. Two years later Freund and his co-workers[2] demonstrated similar inflammatory nodules in the nerve sheaths of patients with rheumatoid arthritis, and they followed up this work by confirming the results of Curtis and Pollard.[3] In this country Gibson, Kersley,

[11] *Amer. J. Syph.*, 1948, **32**, 115.

[1] *Ann. int. Med.*, 1940, **13**, 2265.
[2] *Amer. J. Path.*, 1942, **18**, 865.
[3] *Science*, 1945, **101**, 202.
[4] *Ann. Rheum. Dis.*, 1946, **5**, 131.
[5] Ibid., 1948, **7**, 132.

and Desmarais carried out a series of similar investigations and showed that the pathological lesions in muscle were of two kinds: (1) pericapillary collections of lymphocytes, plasma cells, and sometimes eosinophils, between the muscle fibres; and (2) paravascular collections of lymphocytes only, associated with sclerotic arterioles in the perimysium. They also found similar lesions in the perineurium of the radial nerve and in the fat surrounding the synovial membrane of the knee-joint.

More recently the same authors[5] have examined biopsy material obtained, not only from patients with rheumatoid arthritis, but also from patients suffering from joint pains caused by other conditions, which included non-specific polyarthritis, post-gonorrhoeal arthritis, acute and subacute rheumatism, osteoarthritis, spondylitis ankylopoietica, gout, and Still's disease. Fifteen non-rheumatic patients were used as controls. The patients with polyarthritis were divided into two groups, one with a diagnosis of idiopathic rheumatoid arthritis and the other with a diagnosis of non-specific infective arthritis. Typical lesions were found in the muscles of 34 of the 56 cases in the former group (60.7%), but their incidence appeared to have no relationship to the activity of the disease as estimated by the severity of the symptoms, muscle wasting, or the blood sedimentation rate. The duration of the patients' symptoms, however, seemed to be a more closely connected factor. Clear-cut negative results were obtained in spondylitis ankylopoietica, rheumatic fever, and post-gonorrhoeal arthritis, as well as in the fifteen non-rheumatic controls. Out of the seven cases of osteoarthritis and the five cases of gout there was only one doubtful muscle lesion in each group; in the four cases of non-specific infective arthritis there were changes in muscle and synovial membrane in one, and in the synovial membrane only in two; there was a muscle lesion in one of the three cases of Still's disease and a skin lesion in another; and out of the four cases with subacute rheumatism and cardiac involvement a skin lesion only was found in one.

These lesions, therefore, are not specific, but occur in a significantly high proportion of cases of rheumatoid arthritis, hardly at all in osteoarthritis, and not at all in spondylitis ankylopoietica. Kersley and his colleagues suggest that muscle biopsy might be used as an aid to diagnosis in difficult cases, but since muscle lesions were found in less than two out of three of their patients with rheumatoid arthritis it is difficult to see what significance a negative finding would possess. The value of the work lies in its demonstration that rheumatoid arthritis is not localized to periarticular tissues but is a disease causing widespread pathological changes in mesodermal tissues, of which lesions in muscle are only a part. The negative results obtained from muscle biopsies in the case of osteoarthritis and spondylitis ankylopoietica suggest that the origin of these diseases differs from that of rheumatoid arthritis.

[5] *J. Lab. clin. Med.*, 1947, **32**, 1045.

RADIATION AND LYMPHOCYTES

A method of detecting changes in the blood of persons exposed to ionizing radiations has been described by Dickie and Hempelmann.[1] They carried out blood examinations on 364 individuals, 195 of whom were either exposed to small doses of various kinds of radiation, or worked with radioactive material, or were exposed to uranium in the form of oxide fumes; the remaining 169 individuals were not so exposed, and acted as controls. Using supravital staining methods, they recorded the presence or absence of neutral red granules (Gall's granules) in the lymphocytes, and they were able to show that in the lymphocytes of the individuals exposed to radiation and uranium fumes abnormally large numbers of these granules were present before any change in the total lymphocyte count occurred. In order to obtain satisfactory preparations the authors had to use stronger solutions of dyes than are customarily employed, and they found that phase-contrast microscopy was of much assistance in detecting the inclusions, which they believed to be granular in composition. Analysis of their findings also showed that there was a significant reduction in the total number of leucocytes in the workers exposed to radiations compared with the individuals in the control group. If the results of this research are confirmed, a further method of checking the health of workers in these dangerous occupations will be available.

THE TREATMENT OF NOMA

Noma, or cancrum oris, is fortunately rare in Western Europe, though during the war it was not uncommon among those confined in internment camps. It can still be seen in children and occasionally in adults in Africa, South America, and India, and in the last country it sometimes occurs as a complication of kala azar. Its exact aetiology is not known, but the associated infection is due to spirochaetes and fusiform bacilli, accompanied by diphtheroids and streptococci—organisms also present in tropical ulcers, ulcerative stomatitis, and Vincent's angina. If these organisms are removed the lesions heal. A decrease in the numbers of polymorphonuclear leucocytes, such as occurs in inanition and agranulocytosis, appears to be an essential precursor of noma. Good results were occasionally obtained with local applications of cod-liver oil or with sulphonamides,[1] but in 1944 Findlay, Hill, and Macpherson[2] reported the successful treatment with parenteral penicillin of two cases of noma in tropical Africa. Confirmation of the value of penicillin came from Benhamou and his colleagues[3] in North Africa, who successfully treated five cases, and from Vaizey,[4] who cured two children and one adult in Ethiopia. Among the starving prisoners in Belsen there were several with noma. Dawson[5] treated five patients with penicillin intramuscularly and sulphonamides and penicillin locally. Four were cured, but one did not respond to this treatment. For children 300,000 units of penicillin in three days would appear to be a minimal dose. The results are often quickly apparent, as in the case recently reported by Dr. D. Mackay[6] in this *Journal*, in which improvement was obvious within 24 hours. Dana and his colleagues[7] used penicillin to cure a child who developed noma after being treated for syphilis with bismuth. There have been similar good reports from many parts of the world,[8-16] but it sometimes happens that although the lesions clear up and the toxaemia decreases the patient may die from the extreme inanition which is probably responsible for the onset of noma. Only one failure to respond to penicillin treatment has so far been recorded, and it is clear that the mortality of noma, previously a very fatal disease, can be reduced to negligible proportions.

[1] La Scala, F., *An. paulist. Med. Chirurg.*, 1945, **49**, 523.
[2] *Nature, Lond.*, 1944, **154**, 795.
[3] *Algérie méd.*, 1946, p. 264.
[4] *British Medical Journal*, 1946, **2**, 14.
[5] *Brit. dent. J.*, 1945, **79**, 151.
[6] *British Medical Journal*, 1949, **1**, 223.
[7] *Bull. Mém. Soc. méd. Hôp. Paris*, 1945, **61**, 348.
[8] Klossner, A. R., *Ann. chir. gyn. fenn.*, 1946, **35**, 5.
[9] Sen Gupta, P. C., and Chakravarty, N. K., *Indian med. Gaz.*, 1945, **80**, 542.
[10] Chaudhuri, K. C., *Indian J. Paediat.*, 1946, **13**, 124.
[11] Dajani, M. T., *J. Palestine Arab. med. Ass.*, 1946, **1**, 183.
[12] Alvarez Sainz de Aja, E., *Acta derm. sif.*, 1946, **38**, 270.
[13] Pernetta, C., *et al.*, *Hopital, Rio de Janeiro*, 1945, **28**, 709.
[14] Carnevale, A., *Pediatria*, 1946, **54**, 303.
[15] Tupas, A. V., and Jongco, A. P., *J. Philippine med. Ass.*, 1946, **22**, 153.
[16] Shrand, H., *Clin. Proc.*, 1947, **6**, 197.

ISRAEL'S BEVERIDGE PLAN

NEW HEALTH SERVICES

The Beveridge Plan of 1942 aroused great interest in Palestine, especially among Jewish Agency leaders, who were then working on the assumption that they would form the nucleus of a Cabinet when Jewish independence was achieved. The Beveridge report was immediately translated into Hebrew by Mr. I. Kanievsky, an expert on social welfare and administration.

Social insurance in Palestine is exactly as old as it is here. In 1912, while Lloyd George was initiating national health insurance in this country, the *Histadruth*, which is the trade union confederation embracing most Jewish workers, founded its *Kupat Cholim* or sick fund. The pioneers in this movement were a handful of agricultural workers in Judaea and Galilee who were opening up a desolate and undeveloped area. Palestine was still under Turkish rule; settlers were rare birds distrusted not only by the Arabs but also by the old Jewish population in the towns. Such medicine as there was in this environment was synonymous with witchcraft, though probably less honoured. From these beginnings there developed a comprehensive health service covering 75% of all Jewish workers in Palestine, all paying a unified contribution according to earning capacity. Under the aegis of the *Histadruth* there were established health insurance schemes providing maternity benefit, an invalid fund, unemployment fund, and old age, widows', and orphans' funds.

Health services in Palestine, however, suffered from the lack of a single co-ordinated system of insurance. Many Jewish bodies outside the General Federation of Labour provided facilities that did not always work in harmony with the main organization, and many schemes were still dependent on outside charity. The British were themselves developing social services to include the Arab population, which in Palestine was perhaps served better than anywhere in the Middle East. Some Arabs came within the framework of the *Kupat Cholim*, especially where Jews and Arabs were employed together. In these cases Arab workers received medical care against compulsory payments by their employers.

The Kanievsky Plan

A Cabinet subcommittee is now working on draft proposals to centralize these different schemes so as to include all the citizens of Israel. Administration will be the responsibility of the Ministry of Social Welfare under Mr. I. M. Levin, the Minister, a comparatively new immigrant to Israel who escaped from the Warsaw ghetto. This special subcommittee has the task of putting the "Plan for Social Insurance in the State of Israel," commonly called the Kanievsky Plan, into operation. This plan was first submitted to the *Histadruth* executive, which sponsored the research, in May, 1948. It includes the following main points:

1.—Free medical aid, including hospital treatment, for all citizens of Israel.

2.—Compulsory social insurance for all wage-earners, including members of the free professions, artisans, etc.

This insurance scheme will include medical treatment; workmen's compensation; special allowance for expectant mothers and maternity aid; assistance to invalids; unemployment insurance; old age pensions and assistance to widows and orphans. According to the original plan the scheme will be financed from contributions by employees, employers, and the State. These contributions would correspond to 18% of the employee's wages; 5% contributed by the employee, 8% by the employer, and 5% by the State.

Taking into consideration the rapidly changing structure of Israel's population, which is expected to be doubled within the next four years, such a plan can be carried out only step by step. The general opinion is that the first step would be the provision of free hospital treatment for the whole population. At present the available accommodation in Israel's civilian hospitals is only 2 beds per 1,000 population. However, there are a number of military hospitals which should soon be at the disposal of the Government. In addition, the Government and existing medical organizations are already considering plans for the early establishment of many new and modern hospitals, and to this "capital investment" it is expected that the Jewish Agency, the international Zionist fund-raising organization, will make its contribution.

In implementing this scheme it is not intended to abolish the present status of physicians in private practice. A large proportion of the country's medical profession may find employment in these Government schemes, but the remaining private practitioners will not lack work.

The Cabinet subcommittee, headed by Mr. Kanievsky, is composed of the Directors-General of the Ministries of Finance and Health and Social Welfare, three specialists whose experience during the Mandate and in the government departments of other nations should prove valuable. The main employers' associations have not yet had time to consider the plan officially and so far have not made their views known. But in view of the fact that such schemes are already in operation in almost all progressive countries it is believed that opposition to the plan will not be too strong, although some of the employers' representatives feel that the introduction of such a comprehensive plan may be premature.

WOUNDED AND SICK PRISONERS OF WAR

DRAFT RED CROSS CONVENTIONS

A Red Cross draft convention which the diplomatic conference referred to last week (p. 768) is studying at Geneva lays down regulations concerning the mixed medical commissions appointed on the outbreak of hostilities to examine wounded and sick prisoners of war. Each of these commissions is to be composed of three members—two belonging to a neutral country (one of whom is to be the chairman) and the third to the detaining power. The neutral members are to be appointed by the International Committee of the Red Cross and approved by the two belligerent powers. If possible, one of the neutrals should be a physician and the other a surgeon. They are required to be entirely independent of the warring powers, which must grant them all facilities in discharge of their duties, including a visit to each prisoner-of-war camp at intervals not exceeding six months. These mixed medical commissions may either propose repatriation or may refer a prisoner for a later examination, and the detaining power is required to carry out these decisions within three months. A proposed regulation not in the existing (1929) Geneva Convention for the Wounded and Sick is that prisoners of war who, in the opinion of the medical authorities of the detaining power, are manifestly in a serious condition shall be repatriated without having to be examined by the commission.

Prisoners of war who are to be repatriated direct, according to a draft model agreement which has been drawn up, include all wounded prisoners suffering from lesions equivalent at least to the loss of a hand or foot, and all sick and wounded in whom recovery appears to be unlikely within a year. Prisoners of war eligible for accommodation in a neutral country include those who have better chances of recovery in such a country than in captivity; those suffering from any form of tuberculosis and whose treatment in a neutral country is likely to lead to recovery or to considerable improvement; those suffering from other conditions in which treatment would clearly have better results in a neutral country; those who have undergone a nephrectomy as prisoners; cases of osteomyelitis latent or on the way to recovery, of diabetes mellitus not requiring insulin, and of exanthematic typhus acquired in captivity. Cases of captivity neurosis not cured or on the way to complete cure after three months in a neutral country are to be repatriated. Excluded from accommodation in a neutral country are all cases of duly verified mental affections; prisoners with nervous affections, whether organic or functional, considered to be incurable; chronic alcoholics; and all cases of contagious disease during the infective period, with the exception of tuberculosis.

A list of conditions has been set out in which the decision of the mixed medical commission must be based to a great extent on records kept by camp physicians and prisoner doctors of the same nationality, or on an examination by medical specialists of the detaining power. These include chronic asthma and bronchitis, chronic cholecystitis, serious chronic diseases of the central and peripheral nervous system, and auditory disorders, such as total unilateral deafness, if the other ear does not discern the spoken word at a distance of one metre.

Marking of Hospital Ships

Some work on the visibility of hospital ships has been undertaken by the research laboratory of the Admiralty and laid before the conference. The present convention states that hospital ships shall be painted white and display vermilion red crosses, three of them, of a height of three metres, on each side of the hull, two others in a horizontal position so as to be plainly visible from the air, and two more vertically above the main deck, one to be seen from astern and the other from ahead. During darkness or reduced visibility the crosses on each side of the hull are to be floodlit and the crosses on the superstructure to be made luminous by means of lamps. There are also provisions for an automatic switching mechanism to give flashing or alternating illumination.

The Admiralty experiments suggest that these devices may not be the best possible. In daylight, at the range at which a ship is first seen, there is no possibility of identifying a vessel as a hospital ship. In many cases the range must be halved before recognition is possible, and sometimes, as with the white hospital ship of the Geneva convention, which is most difficult to identify because it can easily be confused with a warship painted a light grey, the range must be reduced to one-third or one-quarter before identification can be certain, and even then the first recognition is not of the painted red cross. The proposal is that a hospital ship should be painted black and light yellow (or white) on either side of a vertical line drawn at the mid-point of the length of the ship, and that the black half should carry a yellow or white cross and the yellow or white half a black cross. With such a design the unmistakable half-and-half pattern first shows itself, and the crosses appear later. The object of introducing yellow, with its high reflectivity, is to obtain any advantage due to colour. Some complicated experiments have been carried out on the required dimensions of the cross if it is to be seen under varying conditions of meteorological visibility. Under some conditions if the cross is to be seen at all it would have to be of a height which is usually impracticable. The only recommendation on the point which can be made is that the cross should be the full height of the freeboard of the ship and larger if possible. The most conspicuous cross is one which has a thickness of limb equal to one-quarter of its height, and a red cross must be about 10% larger than a black cross to give equal ease of recognition under the same viewing conditions.

For visibility of hospital ships at night the Admiralty workers advise against floodlighting, and consider that luminous signs are preferable. However well floodlighting may be arranged, a red cross on a white ground will at a distance, if any atmospheric haze is present, give a whitish glow with few distinguishing features. The better plan is to use diffusing glass with rows of lamps behind it.

Preparations and Appliances

EXPULSION OF VACCINE LYMPH FROM CAPILLARY TUBES

A MEDICAL OFFICER OF THE MINISTRY OF HEALTH writes: Anti-smallpox vaccine lymph is now put up in capillary tubes which are not of uniform size, and the special device that used to be sold for expelling the lymph from the tubes is not always readily available and is sometimes ineffective. A simple alternative is to use a baby's feeding-bottle teat, the open end of which is easily occluded by the thumb. The teat can be sterilized by boiling, and the nipple hole is usually about the right size to make an airtight joint with a capillary tube.

Another method, suggested by Dr. O. H. Bowen, of Kingsbury, N.W.9, is to break off both ends of the lymph tube and then to insert into one of the open ends the sterilized needle of a hypodermic syringe with the plunger pulled out. If the junction of tube and needle is surrounded by a small sterile pledget of wet cotton-wool to make an airtight joint the lymph can be expelled without difficulty by pushing down the plunger of the syringe. It is obvious that care must be taken to sterilize needle and syringe before they are used for other purposes.

Reports of Societies

PATHOLOGICAL TESTS IN RHEUMATIC DISEASE

A meeting of the Section of Physical Medicine of the Royal Society of Medicine on April 13 was devoted to a discussion of the significance of pathological tests in rheumatic disease. The president, Dr. L. C. HILL, was in the chair.

Dr. D. H. COLLINS discussed the contribution which the histologist or cytologist could make to the diagnosis and management of the patient who presented himself at the rheumatism clinic. Investigations requiring the removal of material by aspiration or excision biopsy were not applicable in all cases, but where they could be employed usefully direct information about the pathological process could often be obtained.

If the fluid in an acutely inflamed joint was withdrawn and examined, septic arthritis could be identified by the presence of pus and organisms. Traumatic effusions always contained either blood or blood pigments. Many investigations had been made on the mucin content of synovial effusions. Although generally the mucin content and viscosity of an inflammatory effusion were low and of an effusion due to osteoarthritis high, this examination was of little value in differential diagnosis, because it was never known to what extent the bulk of the effusion was contributed to by watery transudate.

Synovial biopsy in cases of suspected tuberculous arthritis was a routine procedure. It should be used in all cases of arthritis where there was a possibility of tuberculosis, especially in monarticular disease. A positive histological diagnosis could almost always be made in cases of rheumatoid arthritis when the following five features were found together: hyperplasia of the synovial membrane and villi; hyperplasia of the synovial lining; massive lymphocytic or plasma-cell infiltration; inflammatory hyperaemia and oedema varying in degree with the duration and intensity of the inflammatory process; and absence of other specific histological characters. This histological diagnosis of rheumatoid arthritis must be considered, of course, in relation to the clinical features, but he was sure that it had prognostic value and probably diagnostic value, even in the monarticular case; but unless the five features were clearly recognizable the diagnosis of rheumatoid arthritis was not justified.

Relative Viscosity of Blood Plasma

Dr. H. J. GIBSON confined himself to a discussion of the relative viscosity of blood plasma in comparison with other empirical tests of rheumatic disease. The estimation of plasma protein changes was of value in diagnosis, especially in the rheumatic group, and in the objective assessment of activity. Such estimations were also important tests of cure. The blood sedimentation rate had been the sheet anchor in investigation; it had stood the test of time, and there must be few rheumatism clinics in which it was not used extensively. Its advantages were the ease with which it was carried out and the understanding they had of its interpretation. The disadvantage of the blood sedimentation test was that it was an indirect estimation: a plasma abnormality was tested for by the effect on a second reagent—namely, the red blood cells. Plasma was already a very complicated physico-chemical system, and when red blood cells were added the picture became still more complicated. If a test could be found which would eliminate the use of red cells and would estimate abnormalities in the plasma directly, a great advance would be made. A formalin gel test and a colloidal gold test had been described. The latter might be positive in about 75% of cases of rheumatoid arthritis—a strongly positive reaction being found only in about 50%—but this test did not correlate well with the blood sedimentation rate. It appeared to estimate a different abnormality, although both abnormalities might be the result of the disease.

The increase of plasma viscosity was an old observation, but recent work had revived interest in it. The test was applied first in cases of tuberculosis, and a high correlation was found between clinical activity and the viscosity zone—a rather narrow zone—associated with pleural effusions. It was found in tuberculosis that normal viscosity might be found first in the

early stages and later in remissions, and also, rather paradoxically, in the terminal stages of the disease.

This work seemed to be of interest as proposing a relatively simple test which might replace the blood sedimentation rate or supplement the information it afforded. It was an estimate of the viscosity of plasma relative to distilled water, carried out at 20° C. with undiluted oxalated plasma. Dr. Gibson showed the results obtained in 365 observations on 286 cases of rheumatoid arthritis, the relative viscosity and the sedimentation index being correlated. The activity of the disease was reflected in the results with both tests, though detailed correlation was difficult to discern. In this series of cases, if the blood sedimentation rate only was examined, abnormalities shown by viscosity readings would have been missed in 13 observations, and if the viscosity only had been taken abnormalities shown by the blood sedimentation rate would have been missed in 20 observations. Abnormalities were demonstrated by both tests in 94.2% of the observations. There was thus an advantage in carrying out both tests if the maximum abnormality was to be ascertained. The inferences to be drawn from the tests were concurrent, and yet the tests were not testing quite the same thing.

Indeed, the value of the viscosity test was that it did not appear to be estimating the same abnormality as the blood sedimentation rate. The abnormalities were different, or at least were different facets of the same plasma abnormality. He was not advocating that the blood sedimentation rate be abandoned. There was a place for both tests, especially in cases where it was desired to have close supervision and control, as, for example, in therapeutic trials. If there were two different indices of improvement or deterioration to hand to the statistician it was a great advantage. The tests should be regarded as complementary.

Asked whether the cases in which there was a discrepancy between the relative viscosity and the sedimentation rate had been checked back clinically to exclude the possibility of some other infection such as a cold or influenza, Dr. Gibson explained that it was not a single observation which was made in these cases, it was a follow-through observation, and the discrepancy existed throughout. He added that he had avoided mentioning individual cases, because in rheumatism "almost anything can be proved by selecting your cases."

The brief ensuing discussion, in which Dr. W. S. TEGNER, Dr. J. HARKNESS, and Dr. COKE participated, was mostly concerned with the types and use of viscometers and the desirability of standardization.

ULSTER PAEDIATRIC SOCIETY

The inaugural meeting of the Ulster Paediatric Society was held in the Royal Belfast Hospital for Sick Children on April 5. Dr. ROWLAND HILL was elected chairman, and Dr. W. A. B. CAMPBELL honorary secretary. The main business of the meeting was to draw up the constitution and rules of the Society, after which the film "Patent Ductus Arteriosus" was shown. It is planned to hold at least three clinical meetings in each year.

A meeting of the North of England Obstetrical and Gynaecological Society was held in the Jessop Hospital, Sheffield, on March 18, with the president, Mr. S. B. HERD, in the chair. Mr. O. V. JONES, of Bangor, described a case of hydatidiform mole. The pathological findings in this case were discussed by Dr. G. EVANS. Dr. C. G. PAINE described a case of haemolytic disease in a newborn child with group A Rh-positive blood, the mother's blood being group O Rh-positive. Mr. P. MALPAS reviewed the gynaecological aspects of regional ileitis.

The Nurses and Midwives Whitley Council announces that it has agreed on the following revised rate of remuneration for student district nurses: £140 per annum plus emoluments valued at £100 per annum, or a living-out allowance of £100 per annum for non-resident students. As this is part of the student-nurse settlement, which came into operation on Sept. 1, 1948, the new rates will apply retrospectively to that date. If in any case an existing student would receive a lower rate of remuneration under these arrangements than before, the present rate may be continued on a personal basis. The new rate is provisional and may be revised. The rate previously paid to student district nurses in training for the certificate of the Queen's Institute of District Nursing was £95 per annum plus emoluments valued at £100 per annum.

Correspondence

An Unfortunate Precedent

SIR,—The fear of favouritism in respect of the Awards Committee is probably quite unfounded and, in the case of Lord Moran, of course ridiculous. But it seems to me that the ideal future composition of such a committee would include a chairman who was not a medical man at all but either an eminent jurist used to weighing evidence or a Fellow of the Royal Society of accepted standing and experience. The presidents of the Royal Colleges should be *ex-officio* members while in office, and the other members of the committee should be elected annually, biennially, or as seemed most practicable. This would minimize, if not abolish, any fear of favouritism and would probably also be acceptable to such people—of whom I happen to be one—as believe that the Royal Colleges should be mainly concerned with preserving and fostering the educational and ethical standards of the profession and not meddle—*qua* colleges—with such questions as salaries, fees, and mileage.—I am, etc.,

Easton Royal, Wilts. H. H. BASHFORD.

SIR,—Your courageous and pertinent leading article (April 23, p. 717) on the above has produced an undignified reply from the inner cabal of the Royal College. The eight signatories of this reply not unnaturally regard themselves as the henchmen or bodyguard of their President; but in their haste to express their sharp resentment of your free criticism they expose the weakness of the regulations by virtue of which they hold office. And it is to these weaknesses that I wish to address myself rather than to the question whether you had not expressed simply and clearly what so many of us have felt and thought.

I wonder if the general body of practitioners, including the large number of Members, realize how the R.C.P. is actually governed in practice, or how much of their professional life is affected by the senior Royal College. Put as briefly as possible, it is as follows. In theory the whole body of Fellows rule and govern the College. In practice they do nothing of the kind. So archaic are some of their procedures that even to the present day the assembled Fellows at the meeting of the Comitia for the election of a President are solemnly presented each with a half-crown. By all means revere and venerate long-established custom when no harm is done thereby. But this ancient custom is merely a reminder of the time when the College of Physicians was essentially the College of the Physicians of London and attendance by the great majority could be expected.

It is still the rule that those actually present and voting are the only Fellows who can elect the President. But to-day Fellows of the highest repute and learning live and direct the studies of rising generations in parts of the world not even discovered when the charter of the Royal College was granted. These have no say or place in framing the policy of the College, nor have they even a representative committee, and still less nominees to the Council of the College. Are these exponents and judges of good medicine to be excluded merely because some rule was laid down before their country was known to exist?

From this one defect comes the majority of all the other defects in the College constitution. Once the President is re-elected the cabal reassumes its hold on all policy; and by diffusing an atmosphere of "Touch not established custom" subsequent meetings of the Fellows in Comitia all too often become formal and routine acceptance of the Council's recommendations. It is true that printed agenda are circulated to every Fellow containing the recommendations of the Council, and that these recommendations are technically open to discussion. But to question these instantly produces a sense of trespassing on strictly preserved coverts and using time that will produce no change.

What is the obvious result of such an atmosphere? It is and must be that unless a Fellow is *persona grata* to the inner

council, however good a counsellor he may be, or however anxious to give his best to the College, there is no probationary forum where he could be welcomed and tried out, and so he will probably remain outside. It is equally obvious that the whole body of Fellows scattered all over the world cannot run the day-to-day business of the College. But there is much room between the two extremes for moderate and sensible development without offence to our ancient foundation. In this gap there is ample space to make the rules of the College more consistent with twentieth-century methods of true democratic government.

To introduce changes that would bring the knowledge and advice of a wider circle of Fellows into the policies and development of the Royal College would find an immediate response from many who now realize that they have no means of contributing to these matters and are, therefore, irregular in their attendance at Comitias. The College would then rapidly become the deeply loved and respected head of all that is best in true world medicine. I feel that it is only dormant and waiting to be led back into its true path. Had this been the trend of the last nine years instead of efforts to entrench the established rules and to combine local and parochial medico-politics with the high office of President to which your article refers, then there would have been no occasion for your leading article. The joint position of P.R.C.P. and Chairman of the Awards Committee would have been unthinkable.

There are many other matters besides those that I have raised, such as conditions for the membership examination, that have long called for readjustment to the changed conditions of medicine.

The recent meeting of the Prime Ministers of the Commonwealth and the nature and result of their deliberations give true point to my argument.—I am, etc.,

London, W.1. C. B. HEALD.

SIR,—The reply (April 30, p. 774) provoked by your leading article (April 23, p. 717) on the above subject and published over the signatures of the censors and other officials of the Royal College of Physicians will doubtless provoke much correspondence. May I, as a surgeon with no personal interest in merit awards, say that I believe you, Sir, in your article to have voiced the real views of the consultants and specialists in the country?

It is quite obvious to me that the gentlemen who have written the reply are, like too many distinguished members of the profession, completely out of touch with the realities of the situation that faces us and with the opinions of the rank and file of specialists. "The sympathetic attitude of the Minister of Health"—the expression is almost humorous, if the situation were not so serious. "Terms of service which are considered by most consultants and specialists to be just and generous"—when the truth is that most consultants and specialists are seriously perturbed and gravely dissatisfied with those terms, *when they are examined intelligently*.

Like some of the signatories, I am getting on in years, but I am not yet in my dotage and I *do* go to meetings and listen to the views of my younger colleagues. Whilst I appreciate the loyalty which rallied these gentlemen to the defence of their President, I tremble for the future of my profession when those who should be among its leaders are obviously so gravely misled as to the facts which face us and as to the feelings of their colleagues. I would beg them all to read, mark, learn, and inwardly digest your leading article at p. 762 of the *Journal* of April 30. Surely that will open their eyes a little.—I am, etc.,

Southport. R. R. M. PORTER.

SIR,—If the fears expressed in your leading article (April 23, p. 717) and "Young Specialist's" letter (April 30, p. 774) are well founded the moral condition of our profession is such that the particular composition of an Awards Committee seems of small importance. The picture of the President on the one hand dispensing "awards for the boys," and a group of aspiring young specialists on the other silently stifling their valuable criticism or warm-hearted admiration with a weather eye on the awards barometer, should certainly cause concern; though I suspect the reaction may generally be a rather more light-hearted one.

I do not share your pessimism, but fear that arguments of this sort if taken seriously may encourage faction at a time when harmonious unity for the main purposes of our profession is more important than it has ever been.—I am, etc.,

Oxford. C. W. M. WHITTY.

The Intervertebral Disk

SIR,—Mr. Michael Kelly misquotes me in his letter (April 23, p. 725) on the subject of the intervertebral disk. In the Mackenzie Lecture, an abridged edition of which was published in the *Journal* of Feb. 12 (p. 255), I did not say that "when a stooping man begins to extend his spine the posterior margin of the disk is compressed. . . ." This would imply that this condition invariably happened. In fact, it is only in exceptional circumstances, as I was at pains to prove, that this circumstance does arise.—I am, etc.,

London, W.1. HUGH E. GRIFFITHS.

Use of the Term "Coliform"

SIR,—The term "coliform" has for some time had an obscure meaning and it has become increasingly clear that a definition is desirable. Those interested in medical and veterinary bacteriology have used it to embrace only the morphological characters of many species, not of *Bacterium coli* alone but of the dysentery bacteria, the salmonella, and other Gram-negative rods similar to *Bacterium coli*. On the other hand, the term "coliform" is restricted by many water and dairy bacteriologists to those organisms which are not only morphologically similar to *Bacterium coli* but which resemble it in its cultural and biochemical characteristics; some have even regarded it as being synonymous with *Bacterium coli* of faecal origin.

Because of this confusion, and also because there is now a closer liaison between all those who study bacteria from whatever aspect, a committee of nine, representing this variety of interests, was appointed by the Society for General Microbiology and by the Society for Applied Bacteriology. This committee met on several occasions and discussed the matter from wide angles, and the relevant portion of their report is quoted below.

1. The term "coliform" means "like *Bacterium coli*," or "coli-like."

2. "Coliform" is an adjective and as such has no generic or ecological significance.

3. It is proposed that the term "coliform" should refer to *Gram-negative rods resembling Bacterium coli in morphology and staining reactions but not necessarily in cultural and biochemical characteristics*.

4. It is hoped that the widest publicity will be given to this definition to prevent the term being employed to define different specific types by different workers, or to restrict the term to particular branches of bacteriology.

The committee are convinced that the proposed definition is the only one satisfactory to all interests in bacteriology and are opposed to any definition based on ecology or biochemical reactions. They hope that bacteriologists in general will understand and agree upon the meaning of the term "coliform." Existing systems allow for classification of organisms grouped under the wide term now proposed.—We are, etc.,

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Royal Veterinary College, London, N.W.1.

C. B. TAYLOR,
(Society for Applied Bacteriology)
Butterwick Research Laboratories,
Welwyn, Herts.

Needle Biopsy of the Liver

SIR,—In his excellent paper on liver biopsy Dr. Richard Terry (April 16, p. 657) recommends local anaesthesia, and this seems to be the usual practice. However, it is worth considering whether this procedure is not better done under thiopentone anaesthesia. During the war years overseas, when mysterious diseases with enlargement of the liver were so common, it

was sometimes desirable to examine material by biopsy of liver, spleen, gland, or marrow before a diagnosis (e.g., of kala azar) could be determined. These procedures are all rather unpleasant, and tend to be associated in some measure with anxiety to patient and doctor alike. It was found that, if needs be, even three to four such procedures could be safely and expeditiously carried out by a team of workers using thiopentone anaesthesia.

There are several advantages : anxiety, pain, or discomfort are eliminated, and the operator is free to concentrate on the various manœuvres without worrying about the patient's feelings. This added confidence also means a surer thrust, and if by any chance no tissue is obtained the puncture can be immediately repeated. Safety is increased, because absence of movement of the patient and his liver can be assured if the sole duty of one member of the team is to press firmly upwards from below the right costal margin, so that the liver is held fast against the diaphragm. The patient is always grouped first, and vitamin K is given no matter what the prothrombin time. Very firm pressure over the site of puncture is maintained for a few minutes as a precaution.

There has been only one untoward incident, and that not directly related to the biopsy. During the early phase of the anaesthetic, when the patient was apparently semi-conscious, he suddenly swung left and dealt the anaesthetist a shrewd blow amidships which crippled him, and then knocked the needle out of my waiting hand with his elbow. An able assistant restored the situation by reinserting the thiopentone needle into the vein whilst the biopsy needle was boiled up again. Liver tissue was then obtained without difficulty.

In this country liver biopsy alone is usually all that is required ; but, if at all likely to be necessary, sternal puncture, for example, may conveniently be carried out at the same time under the same anaesthetic. Many will testify to the satisfactoriness of this technique, which has been used consistently over the past five years.—I am, etc.,

Edinburgh. R. W. D. TURNER.

Herpes Zoster Recurring in a Baby

SIR,—The following case is reported, as it appears to be unusual.

The mother of a baby who was born on April 17, 1948, developed varicella when four months pregnant; she caught this from her daughter, who was attending day school. There were no complications. The gestation was otherwise normal. The child was delivered at full term—a spontaneous breech. She was breast fed for seven weeks and then given modified cow's milk four-hourly.

On June 7, 1948, the child developed a rash on the left side of the chest and back. This I first saw on the following day, when I found a typical herpes zoster with a distribution over the left scapular region, the left lateral chest wall, and the left breast. The lesions were kept dry, and cleared up spontaneously in about 14 days, leaving no scars. During the illness the feeding was changed to National dried milk, on which the child thrived.

On Dec. 29, 1948, the mother noticed a similar rash on the right scapular region. I saw the child the following day and found a similar typical herpes zoster rash distributed over the right scapular region, the right axilla, the right inner arm, and the left forearm and inner side of the wrist. Over the scapula the lesions were few and discrete, but the axilla and arm were covered with confluent patches of vesicles which faded out towards the ulnar border of the hand. At no time did I find any constitutional disturbance: there was no raised temperature, no anorexia, no loss of sleep, no apparent pain. The baby remained just as active as ever.

Vaccination was performed in August, 1948—i.e., about 8 weeks after the beginning of the first attack of shingles. There have been no sequelae.

—I am, etc.,

London, N.19. C. H. JOHNSON.

Diparcol in Parkinsonism

SIR,—The article by Dr. R. S. Duff (April 9, p. 613) has been of great interest to me, as I too have been using the drug for some considerable time. After reading the paper by Sigwald, Bovet, and Dumont[1] I sent for the original French drug "novocainique" (2987 R.P.), and have since been able to continue the treatment for over a year now by the courtesy of the manufacturers of "diparcol" (the corresponding preparation), who kept me supplied until the drug was put on the market.

My experience, I must admit, consists of one case only, but as it is at great variance to that of Dr. Duff, and the result seems to have been more favourable, I feel I should put my own observations on record.

My patient was not a case of post-encephalitic Parkinsonism, but of Parkinson's disease proper (paralysis agitans). Like Dr. Duff, I started with a small amount, but then, according to the suggestion of Sigwald and Bovet, I gradually increased the dosage until the limit of tolerance was reached, which in this case I found to be 3 g. daily (12 tablets of 0.25 g.). Above that dosage the patient became very giddy, whereas a dosage below that amount increased the tremor. As advocated by the French authors, I also gave the patient tab. amphetamine sulphate, 5 mg., one tablet before breakfast and one before lunch. Further, I gave a sleeping-tablet at night, and like Dr. Duff continued for a while with the alkaloids. The results have been most striking. The tremor has disappeared for periods of one or two hours at a time—amounting to a total of about 12 hours per day—and was much reduced in severity.

The patient is a woman aged 64 who has been suffering from Parkinson's disease for about 11 years. It started with an accident, when her hand was caught in a wringer. The symptoms were aggravated during an air raid and two years later by an accident to her husband. At the time treatment was started she was quite helpless, could not walk, and was trembling all day. She was in a state of persistent stupor, did not take any notice of her surroundings, and was unable to remember anything. She had to be carried from her bedroom downstairs. Now, apart from the considerable reduction in her tremor, she is able to walk about, walk up and down stairs, wash up, set the table, cook a little, change her shoes, read a little, and even knit. She is very bright, and can take full part in everyday life.

In conclusion I wish to point out that, apart from the cases of post-encephalitic Parkinsonism, the drug appears also to be applicable in cases of Parkinson's disease. The maximum dosage should be assessed individually by very gradual increases or decreases. It can be much higher than 1 g. (given as maximum dose by Dr. Duff), as proved in my case, where the optimum dose was 3 g. Drowsiness, cramp, and depression in the initial stages seem to be controlled by the addition of amphetamine sulphate, which is well tolerated by patients with Parkinson's disease. Indeed, these side effects seem to be more pronounced with the smaller dosage, and disappear as the amount of diparcol is being increased.—I am, etc.,

Spennymoor, Co. Durham. E. BRAUER.

REFERENCE

1 *Rev. neurol.*, 1946, **78**, 581.

Vertigo and Influenza

SIR,—Dr. A. H. Gregson (April 16, p. 683) mentions vertigo as a symptom in some cases of influenza. In the last few weeks I have seen four patients in whom severe vertigo was the presenting symptom, and in two of them the only symptom. Whether they were cases of influenza I cannot say, but at the time I regarded them as cases of acute influenzal labyrinthitis.

The first case will serve as typical of the others. He was a man of 70, who came staggering into the surgery as though drunk. He had been perfectly fit the night before on going to bed, but was woken up in the night by violent giddiness. The furniture appeared to be going round from right to left, and when he tried to walk he always fell towards the left side. He vomited and retched the whole night. He had slight nystagmus on looking to the right, but no other abnormalities in the C.N.S. On inquiry, he admitted to a fairly severe lumbosacral backache and a frontal headache, but had no other influenzal symptoms. Temperature and pulse were normal. The vertigo gradually wore off after some three days, and for a further week he got short attacks if he turned his head suddenly. His wife and daughter went down with typical influenza five days later. It will be seen that the evidence for this being a case of influenzal labyrinthitis rests only on the presence of the concomitant headache and backache, and the fact, which incidentally I prophesied, that other cases of influenza followed in this household.

The other three cases were similar. In all the onset was unexpected; one moment the patient was perfectly well, the next moment he would be hanging on to the furniture to keep upright.

The experience was apparently very alarming. Three of the patients were elderly, and two of them said afterwards that they had thought they were going to die. The fourth was a child of 3, and her mother said that she was terrified during the attack. Three of the four had severe vomiting, and all were very consistent in describing objects as rotating about a vertical axis, and always in the same direction. All tended to fall towards the side to which objects seemed to rotate. After the acute attack, which lasted one to three days, all tended to get minor recurrences on rapid rotation of the head. Two had nystagmus on looking away from the side to which they tended to fall. Subjectively, none complained of deafness. Objectively, one had been stone deaf for years, and two others showed differences in auditory acuity between their two ears, but in view of their ages this was of doubtful significance. The child was not tested. Three of the four occurred in influenzal households, but two of them had no concomitant influenzal symptoms.

In any household in which some members have influenza it is a common occurrence for others to develop either a lumbosacral backache, frontal headache, muscle pains, or giddiness. If one assumes that these are abortive cases of influenza it seems reasonable to suppose that severe vertigo may also occur as the sole manifestation of influenza.—I am, etc.,

Great Dunmow, Essex. PETER A. WALFORD.

Marriage Neurosis

SIR,—Dr. R. Macdonald Ladell (April 9, p. 635) revives the old controversy of E.C.T. versus psychotherapy. There are, I fear, many wrong assumptions in Dr. Ladell's communication. In the first place he appears to suggest that if a psychic stress can be unearthed there is no place for E.C.T. This is really a dangerous doctrine.

Those of us who use E.C.T. daily are often only too well aware of stresses which have at least *helped* to produce, say, an anxiety state or a condition of involutional melancholia. Often the patients themselves are only too conscious of these stresses. (A few days ago I saw two sisters who had both displayed anxiety symptoms from the death of their mother one and a half years ago. Both, I feel sure, will rapidly clear up with E.C.T.) To withhold E.C.T. in such cases could result in much unwarrantable suffering on the part of the patients, not to speak of risks of disaster—e.g., suicide.

E.C.T. intelligently applied, with, whenever possible, the patient's co-operation and after a careful physical and psychological examination, is one of the great boons of modern psychiatry. It can cut short all varieties of anxiety and depression, and in many cases the patient is more efficient mentally after its use than almost at any time in his life. (Old, unnoticed, mild states of depression and apprehension which may have existed for years before the acute breakdown are usually also swept away.) It can be used in extreme old age, and is usually a life-saver in delirious cases, which may be almost moribund on admission. Therefore, because some may use this treatment unintelligently, I would deprecate Dr. Ladell's suggestion that "the advocates of E.C.T. made no attempt to understand the cases and thus were turning their backs on all we have learned about the origins and meaning of neurosis during the last fifty years."—I am, etc.,

Armagh, N. Ireland. ROBERT THOMPSON.

Treatment of Varicose Veins

SIR,—In his letter on the treatment of varicose veins (March 19, p. 500) Dr. H. M. Hanschell sets forth his experiences and disappointments with sclerosing agents. He (and others) describes how recanalization of veins takes place in a high percentage of cases following their apparent obliteration by this method. He goes on to describe an operation which in his hands, over a large series of cases, has given excellent results.

This most interesting letter was answered by Mr. R. Rowden Foote (April 9, p. 635), who, although obviously disagreeing with Dr. Hanschell, fails to put forward any evidence refuting Dr. Hanschell's argument against the use of sclerosing substances, and who instead devotes the major part of his letter to the irrelevancy of ulcer, which Dr. Hanschell never mentioned. He ignores the real point at issue, which is whether or not the injection of sclerosants is justifiable, in view of the high recurrence rate as compared with the very much better results following ligation or extirpation by the method which Dr. Hanschell advocates.

In Mr. Rowden Foote's book on this subject it is stated that 85% of varicose veins treated by sclerosing injections had recurred, and furthermore he accepts figures which show that these recurrences are for the most part due to recanalization of the thrombosed veins. It seems reasonable, therefore, to assume that by removing a varicose vein entirely any recurrence can be due only to the formation of new varices in the superficial venous system—an event which is responsible for only 15–25% of recurrences and eliminates the large group of recurrences due to recanalization.

Dr. Hanschell has described a reasonable operative technique which in his hands has given splendid results, but Mr. Rowden Foote has scorned it on the grounds that this treatment has a long history of failures. Granted the principle of the operation may be associated with lack of success when older operative methods are used, but judging from Dr. Hanschell's results it would appear that his method has overcome most of the disadvantages associated with other operations designed to eradicate this condition and at least is worthy of more consideration than has been accorded to it by Mr. Rowden Foote.

Finally, may I draw attention to the virtues of the operation, which in the past few months I have carried out a number of times? The operation itself is simple, the patient suffers very little pain and the minimum of inconvenience, and the cosmetic results are good. Thus far have I satisfied myself that Dr. Hanschell's claims for this method of treatment are well founded. What percentage of my own cases will recur I cannot know until I have followed them up for some years, but if my results are as good as Dr. Hanschell's I shall be satisfied that sclerosants have indeed a limited place in the treatment of this condition; and this has already become more than a mere suspicion, following some years' experience of injection therapy in treating varicose veins.—I am, etc.,

Dublin. NORMAN RUTHERFORD.

Pressure Cooking

SIR,—The paper by Miss Gweneth M. Chappell and Miss Audrey M. Hamilton (April 2, p. 574) and your annotation (p. 582) on the effect of pressure cooking on vitamins are of topical interest, but consider only one aspect of pressure cooking. Some years ago Dr. P. Kouchakoff described experiments he had undertaken to determine the relationship between cooked food and post-prandial leucocytosis (*Lancet*, 1937, 1, 425). He was able to prove by a large number of tests that post-prandial leucocytosis occurs only after the ingestion of cooked food, but not after the same food consumed raw, and that in order to produce a post-prandial leucocytosis the food has to be heated above 83°–87° C., according to the kind of food.

Kouchakoff therefore assumed that heating of food above the critical temperature of 83°–87° C. produces toxic substances in the food and that the leucocytosis is a defensive reaction against these toxins. Furthermore, he found that no leucocytosis occurs when raw food is consumed simultaneously with the cooked food, as, for example, when eating a raw salad with cooked meat. But when the food has been heated above 100° C., as in the case of canned food or of pressure cooking, no amount of added raw food is capable of preventing the post-prandial leucocytosis. If Dr. Kouchakoff's main thesis is right, then routine pressure cooking should be condemned, even though it does not destroy the various vitamins.

I know that a number of physiologists deny the existence of a post-prandial leucocytosis, but this is perhaps because in their tests they failed to differentiate between raw and cooked food.—I am, etc.,

St. Peter Port, Guernsey. A. ORLEY.

Handling of Corned Beef

SIR,—I have been appalled at the way tinned corned beef, used to make up the meat ration, is served to the public. The procedure in the majority of butchers' shops is to open a large tin of corned beef and place the contents on a wooden cutting board. The same knife used for cutting uncooked sausages, uncooked beef, uncooked mutton, uncooked pork, and slabs

of sausage meat is used, without any attempt at cleaning it, for cutting slices of corned beef. The corned beef is then placed on the weighing-machine plate, which quite normally in a butcher's shop is covered with blood. The corned beef is next, in some cases, wrapped in a small piece of grease-proof paper and placed on top of the raw meat, but in other cases it is placed in direct contact with the raw meat.

The recent Ministry of Food Circular MF5/48, "Cysticercus in Meat," is in my opinion of minor importance compared with the procedure stated above. Most, if not all, raw meat in this country is cooked before consumption by human beings, but cooked corned beef supplied to make up the meat ration is not usually recooked. If parasitic worms or cysts are present in the meat, offal, sausage, etc., and evade the meat inspector during inspection, they will be transferred to the corned beef by knives, by butchers' hands, by the scales, and by contact with the raw meat. In 1941 it was proved after the outbreak of trichiniasis in Wolverhampton that this disease was endemic in the Black Country. I consider that the Ministry of Food and the Ministry of Health should give careful consideration to the serving of cooked corned beef.—I am, etc.,

Solihull, Warwickshire. IAN MCLACHLAN.

Dystocia after Amputation of Cervix

SIR,—With reference to Dr. Robert S. C. Fergusson's letter (Feb. 5, p. 241) and Mr. Walter Calvert's memorandum (Jan. 8, p. 58), I believe that the extensive scarification of the cervix resulting from trachelorrhaphies, and even amputations, done so often for chronic endocervicitis associated with milder degrees of lacerations, can be avoided by resort to the operation known here as the Sturmdorf procedure or tracheloplasty. This is fully described in American textbooks on gynaecology, and involves the cutting out of a conical segment of the cervix, extending if necessary to the level of the internal os. The diseased and infected tissues are thus effectually eliminated and the greater portion of the circular muscular fibres retained. There is little or no scar tissue left to impede adequate dilatation in subsequent pregnancies. I have delivered many women subsequent to this operation without difficulty.

Unfortunately the operation is not well known abroad, but may be recommended in appropriate cases as a way to avoid the dystocia described by your correspondents.—I am, etc.,

New York, N.Y. GEO. W. KOSMAK.

POINTS FROM LETTERS

Temperature Recording

Mr. H. J. RAYNER (London, W.1) writes: As one of the students who performed some of the experiments summarized by Professor Samson Wright (April 9, p. 610) perhaps I might suggest that the common practice in recording temperatures is not so misleading as he indicates. He points out that a thermometer inscribed "half-minute" or "two minutes" will not accurately record the *blood* temperature when kept in the mouth (or axilla or groin) for the time indicated. He also suggests that it is undesirable to have a mark at 98.4° F. (36.9° C.) on clinical thermometers, because the "normal" temperature varies greatly with individuals and with external conditions. The experiments performed do certainly show this to be true, but as regards the clinical assessment of an abnormal temperature they may not be of great importance. In the surgery, the home, or the hospital a "half-minute" thermometer is normally placed in the mouth for one minute, or in the groin or axilla for two minutes, and a reading of over 98.4° F. is then generally considered to be above normal. The reading may not be the same as that of blood temperature, and perhaps if it were then a reading of 100° F. (37.8° C.) might not necessarily indicate pyrexia, but it is a reading taken under fairly standard conditions, and both the doctor and the layman have some idea of what such a reading is worth. I think that a further fact shown by the series of experiments was that in most people in health the average figure was lower than 98.0° F. (36.7° C.)—even when a thermometer was held in the mouth until a steady reading was obtained. For this reason any reading above the "normal" mark on the thermometer could be considered as abnormally high, except late in the evening. Personally I should favour retaining both the "half-minute" or "two minutes" inscription and also the mark at 98.4° F., because I think that a reading above this mark obtained in the time indicated does show an abnormal temperature.

Obituary

A. E. BARCLAY, O.B.E., M.D., F.R.C.P.

Dr. A. E. Barclay, who died at Oxford on April 26, was one of the outstanding figures in the world of radiology. Barclay of Manchester, as he was often known, though the later years of his life were spent at Oxford, was interested in every aspect of radiology. His special subject was the radiological study of the alimentary canal, on which he published papers as early as 1912. He was too young to be one of the original founders of the Roentgen Society, but he can be said to have belonged to the second rank of pioneers, eagerly interested in the rapidly opening field of radiology in the early decades of this century. He was one of those who saw the necessity for ensuring that those who set out to use *x* rays in medicine had the proper background of knowledge and the required standard of skill in the interpretation of what they saw. Barclay had much to do with the establishment of training courses in radiology and with the integration of this new discipline in the medical curriculum. He played an important part in the setting up of the diploma in medical radiology and electrology at Cambridge, which he himself took in 1921, and for which he was examiner for many years. His voice was heard more and more often in the counsels of radiologists in those early years. In 1919 he was elected president of the Electrotherapeutic Section (now the Section of Radiology) of the Royal Society of Medicine. He was president of the Roentgen Society in 1924, and, after the reorganization, president of the larger body, the British Institute of Radiology, in 1931. His work was recognized beyond the confines of this country, as attested by his honorary fellowship of the American College of Radiology and his honorary membership of many radiological societies in the Dominions and elsewhere. It was not only his scientific ability which brought him to the front rank, but also his attractive personality and his readiness on all occasions to help colleagues and juniors.

Alfred Ernest Barclay was born in Manchester on Sept. 30, 1876. He went to the Leys School, Cambridge, and from there to Christ's College. His clinical years were spent at the London Hospital, and he graduated in 1904. He was house-surgeon and clinical assistant in the aural and skin departments at the London Hospital, and it was probably his assistantship in the electrical department there and in the Finsen light department which aroused his interest in radioactivity. Barclay proceeded M.D. in 1912, and many years later, in 1937, he was incorporated D.M. at Oxford. In 1935 he became a member, and six years later was elected a fellow, of the Royal College of Physicians. Early in his career he returned to Manchester, where he became a consultant in radiology in private practice and honorary radiologist to the Manchester Royal Infirmary, with charge also of the *x*-ray department at Ancoats Hospital. He was appointed lecturer in radiology to Manchester University, and later held a similar position at Cambridge. The Nuffield Institute for Medical Research was established at Oxford in 1935 for the study of clinical, physiological, pharmacological, and anatomical problems by means of radiological and allied techniques, and Barclay was appointed honorary radiologist, serving also for a time during the war as acting director of the Institute. Here he collaborated in some important work with Trueta and others. It was in 1946 that Trueta, Barclay, and their colleagues demonstrated the renal shunt which may carry such a high proportion of the arterial blood into the renal vein that the cortex is left too anaemic to function properly. Subsequently, in spite of his serious illness, Barclay continued this work and applied the same technique of microradiology of injected blood vessels to the study of the human stomach. In collaboration with F. H. Bentley he was able to show what appears to be the same type of arterio-venous shunt in the gastric submucosa. Their work on this subject was published as recently as February of this year.

During the first world war Barclay served as a captain, R.A.M.C., and during the second world war he was consultant adviser on radiology to the Ministry of Health, and travelled all over the country inspecting hospital departments. His published work was chiefly on the application of *x* rays to the study of the abdominal viscera. In 1912, with W. J. S. Bythell,

a fellow radiologist of Manchester, he published *X-ray Diagnosis and Treatment*, for many years a standard textbook on the subject. *The Digestive Tract: A Radiological Study of its Anatomy, Physiology, and Pathology* appeared in 1933, and there was a second edition in 1936. He was the author of many other publications in British and foreign medical journals. In 1920 at Cambridge, and again in 1930 at Melbourne, he was president of the Section of Radiology at the B.M.A. Annual Meeting.

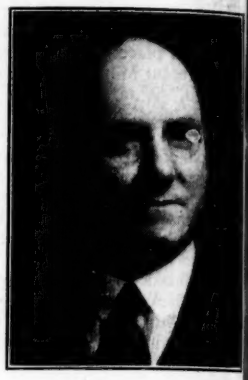
Barclay had been chosen to deliver the Mackenzie Davidson Memorial Lecture under the auspices of the British Institute of Radiology in March, 1949, but when the time came he was far too ill to do so, and the Institute as a mark of respect to him met only for formal business, arranging no other event to take the place of the expected lecture. Its president travelled to Oxford to present him with the lecturer's medal, and brought back a story of a long and painful illness most bravely and cheerfully borne. It was characteristic of Barclay that within two days of his second operation he was sitting up in bed tracing out on paper exactly what the surgeons had done to him. The university of his native Manchester intended to confer on him the honorary degree of D.Sc. on founder's day, May 18. The D.Sc. of Oxford was conferred on him in 1947. In 1946 he was made an honorary member of the Liverpool Medical Institution, and on that occasion the public orator described Barclay as one of the pioneers who had helped to build "a well-fitted dark-room in the house of Medicine." He went on: "Once upon a time he was a Manchester man, but he has long lived that down in the genial air of Oxford. He has given us the work of a master in his book on the radiology of the digestive tract. . . . To craftsmanship he adds a scholar's integrity. He has always taught that the study of the normal is the beginning of radiological wisdom. . . . As Socrates felt about words, so he feels about *x*-ray shadows. To use them in the improper sense is not only a bad thing in itself, but it also generates a bad habit in the soul."

Dr. S. Cochrane Shanks writes: Others will tell the story of Alfred E. Barclay's life. I want to record some aspects of his character that won for him his outstanding reputation as a radiologist and the affection and regard of all who knew him. Barclay was a man irrepressibly good-humoured and benign. It was impossible for a normal individual not to like him. As a consultant adviser in the E.M.S. during the last war he was inevitably subject to occasional ill-informed criticism. I well remember his reaction to one vicious letter: that of sympathetic concern for the state of mind of the writer. It simply didn't occur to him to take offence, and the charm of his personality rallied the radiologists of the country round him when he organized the *x*-ray services of the E.M.S. His success in that task was due also to two other qualities—imaginative enthusiasm and untiring industry; qualities which were also responsible for his deserved reputation as a young radiologist at Manchester and as a researcher in the last phase of his life. The generation who knew Barclay only as a doyen may not appreciate how much he contributed to the radiology of the alimentary tract. His two early books on that subject, published in 1912 and 1914, are classics of their time. In them there is much that is now quaint, but much more that was new then and has stood the test of time. That Barclay, an able young man with an inquiring mind, should contribute to the knowledge of a new and growing subject is not so very remarkable. Many young men have done the same. What is remarkable is that he should, after the age of 60, re-enter the field of research and, in the Nuffield Laboratories at Oxford, lead a team in a series of brilliant anatomical researches on the foetal circulation and on hitherto unknown vascular shunts in the kidney and stomach. Very few have done that. Indeed, alike in youth and in age, he flamed into recurrent brilliance, and radiology is the richer for his long and active life.

SIR SIDNEY SEWELL, M.D., F.R.C.P., F.R.A.C.P.

Sir Sidney Sewell, one of the best-known physicians in the State of Victoria, died on March 13. The prominent part he took from 1928 to 1938 in the formation of an Association of Physicians of Australasia, which led finally to the foundation of the Royal Australasian College of Physicians, will long be remembered. He was Vice-President of the College from 1938 to 1940 and President from 1940 to 1942.

After a brilliant undergraduate career Sidney Valentine Sewell completed his medical course in 1905 and graduated at the head of his year with first-class honours in medicine, surgery, and obstetrics, sharing the exhibition in medicine with G. C. M. Mathieson and winning the exhibition and the Beaney Scholarship in surgery. He was appointed senior resident medical officer to the Royal Melbourne Hospital in 1906, and clinical assistant to medical out-patients in 1910, after his return from two years' postgraduate work in England and Germany. Sewell's public hospital work was almost exclusively confined to the Royal Melbourne Hospital. He became physician to out-patients in 1911, and when he retired in 1939, after nearly thirty years of unremitting service, he was made consulting physician to the hospital. Like many of the senior men, he returned to full duty in the wards during the recent war. Sewell obtained his M.D. in 1910. He became a foundation fellow of the Royal Australasian College of Physicians in 1938, and in 1939 was elected F.R.C.P. He was knighted in 1945.



Sewell's ambition was to follow in the footsteps of his guide and friend, the late Sir Richard Stawell. Sir Richard had set a high standard of medical teaching in Melbourne, based on the best English tradition and practice. Sewell followed his example and never spared himself or his students. His teaching at the bedside will not easily be forgotten by medical practitioners now scattered over all the States of the Commonwealth. The first world war of 1914–18 always held painful memories for Sewell. Owing to a persistent infection following an acute attack of appendicitis in early manhood, his health from his early student days was far from robust. It was remarkable that he subsequently accomplished so much in spite of this constant handicap. He volunteered for active service in the war, but, after more than one medical examination, acceptance for military service overseas was refused on the ground of unfitness. This was a severe blow to him. He served at home and was particularly successful in his treatment of "shell-shocked" cases.

Sir Sidney Sewell had been interested for more than twenty-five years in the management and treatment of tuberculosis. His proclaimed aim was a constructive scheme to wage war against tuberculosis in Victoria so as to stamp it out within a defined number of years. He endeavoured by every means in his power to obtain the co-operation of Federal and State Governments together with the understanding and sympathetic assistance of the community in general. Sewell fought vigorously and uncompromisingly against what he considered to be the apathy, ignorance, and inertia of Government departments on this subject. His crusade was not popular in official circles and it earned him some enmity. He was ultimately effective, however, in arousing general interest in this most difficult problem. He took up vigorously the question of money allowances for public patients during their stay in sanatoria. Here he was in advance of his time in recognizing that often when medical treatment was refused by patients or its acceptance delayed, the reason was financial. He also insisted that treatment when it was accepted lost much of its beneficial effect if the family breadwinner carried with him into the sanatorium anxieties about the financial welfare of his family. Sewell fought strenuously for adequate monetary allowances for these patients, and was rewarded with a considerable measure of success. During the last few months of his life Sir Sidney was recognized by the State Government of Victoria as its unofficial adviser and consultant on questions connected with pulmonary tuberculosis. Official recognition of his work has also been made in the decision to establish "The Sir Sidney Sewell Pathological Wing" in the new sanatorium for 400 male patients, to be erected at any early date at Watsonia, near Melbourne.

Sir Sidney Sewell died from a malignant growth of the lung, which was diagnosed several months before his death. Knowing all the facts, he determined to put his affairs in order and to die in harness. During the final three months, and under increasing difficulties, he was true to his ideals and continued to work for the better management of tuberculosis. Sir Sidney was in the first flight of physicians in Australasia. His knowledge was extensive, his intellectual grasp of medical problems was profound, and he kept well abreast of all major developments in his subject. Many patients and colleagues will mourn his passing and miss his inspiring help in time of need.—C. V. M.

C. W. M. HOPE, O.B.E., M.D., F.R.C.S.

Mr. C. W. M. Hope, consulting surgeon for diseases of the ear, nose, and throat to King's College Hospital, London, died at his home in Knaresborough on April 21 at the age of 68. A memorial service was held at the Hospital Chapel on Monday, May 2.

Charles William Menelaus Hope was educated at Clifton College and the University of Durham, where he graduated M.B., B.S. in 1903. He took the F.R.C.S. in 1908, and proceeded M.D. a year later. After holding three resident appointments at the Royal Infirmary, Newcastle-upon-Tyne, he came to London in 1908, where at first he was resident anaesthetist at St. Mary's Hospital and then clinical assistant to Mr. William Hill in the ear, nose, and throat department. Hope was registrar and later assistant surgeon to the Throat Hospital, Golden Square. In 1914 he was appointed to the honorary staff of King's College Hospital as assistant surgeon for diseases of the nose and throat under the late Sir StClair Thomson. He became the first head of the combined nose and throat and aural departments in 1932, and remained in charge until his retirement in 1941. He was also consulting surgeon to the Finchley Memorial Hospital and the Royal Eye Hospital, Southwark.

Mr. Hope served in the two world wars. In the 1914–18 war he was a surgeon with the rank of major, R.A.M.C., attached to the St. John Ambulance Brigade Hospital, B.E.F. For his services he was awarded the O.B.E. and was made an officer of the Order of St. John of Jerusalem. At the outbreak of the second world war he at once joined the Emergency Medical Service as a full-time surgeon, and he was posted to Horton Emergency Hospital, Epsom, where he worked until continued ill-health led to his retirement in 1941.

Hope was a very fine operator, and all who worked with him, whether as students, residents, clinical assistants, or registrars, will always remember his kindliness, thoroughness, and patience, and his meticulous attention to every detail affecting the welfare of his patient, whether in the out-patients department or the theatre. Until ill-health compelled him to slow down, he was a hard and conscientious worker, and though he did not write a great deal he gave a fine training to all who worked under him, and set an example to students and junior staff that they will always remember. He was interested in all the students' activities of King's College Hospital Medical School, and was associated with the Students' Club and Societies Union for nearly twenty years, first as secretary and later as president. In this work he came into close contact with the students, who always knew him affectionately as "Charlie Hope."

Outside medicine he had many interests, including fishing, gardening, and carpentry. He enjoyed using his hands, in play as well as in work, and no matter what he did he always did it thoroughly. He had a keen appreciation of values and always insisted on the best. His annual holiday was spent in the north of Scotland salmon fishing, and many friends will remember the fine fresh salmon which came to them in late June or early July from Brora. He was a bachelor whose kindliness, generosity, and compelling personality ensured him a wide circle of friends. He will be greatly missed, though never forgotten, by all those who worked under him and learned so much from him.—T. C.

The Joint Committee of the Order of St. John of Jerusalem and the British Red Cross Society has issued its *Register of Ambulance Stations* listing the addresses and telephone numbers where ambulances may be obtained. The service covers many types of cases that do not fall within the ambit of the National Health Service.

Medico-Legal

DEATH FOLLOWING ABORTION

Verdict of Misadventure

At an inquest held at Slough on April 4 and April 13 evidence was given that the death of a girl of 19 was due to shock resulting from an operation for the induction of premature labour.

The mother of Marianne Elise Gotzky said her daughter had not told her that she was pregnant. One day her daughter had turned on the gas. Only after this incident did she confide in the mother, and she said that she would rather end her life than continue with the pregnancy. Her own father, an elderly medical man, arranged for her to take her daughter for examination by a psychiatrist. The psychiatrist had arranged for her to see Mr. Norman Haire and she had given Mr. Haire her own cheque for £150. After her daughter's death Mr. Haire sent her a cheque.

Dr. Ellis Stungo said that he saw Miss Gotzky on three occasions. She was so distressed and unbalanced that he felt she might make another attempt at suicide. He came to the conclusion that her pregnancy should be terminated, and he accepted full responsibility for having advised this. He suggested to the mother that the case was one which would be dealt with by any hospital, but that if she wished he would make arrangements for the girl to be operated on as a private patient. He said that he was paid 12 guineas for these consultations. So far as he knew there were no ill effects following skilled therapeutic interference. It was impossible to treat a patient by psychotherapy in such circumstances. The treatment was the removal of the cause of her symptoms. She could have been admitted to a mental hospital, but he would not have advised that.

Evidence was then given by the night nurse at the Parkside Nursing Home, Upton Court Road, Slough, and by the matron of the home, who explained that she had no certificates and her knowledge of nursing had been acquired by experience. Miss Gotzky was admitted on the evening of April 1 and the operation was performed the following morning. As a general rule, the matron said, she received her fees from the patients, but in this case her account for £7 18s. was paid by Mr. Haire.

The anaesthetist, Dr. Oswald Stuart Thompson, said that the patient was given thiopentone intravenously. He then administered gas and oxygen and a minimum quantity of trilene. The operation took ten or fifteen minutes. He was dismantling his apparatus and packing it away when he noticed that the patient had changed colour and was gasping for breath. Pure oxygen, coramine, and adrenaline were administered, and finally adrenaline was injected into the heart muscle, but without effect. Artificial respiration was continued for probably three-quarters of an hour. The patient had recovered from the anaesthetic to the extent that she was trying to push the airway from her mouth, and her laryngeal reflexes had returned.

Mr. Norman Haire, who reported the death to the coroner, said there was some uncertainty about the period of pregnancy. He judged that the patient was approaching the 28th week and it seemed possible that the child might be saved. For that reason he took good care not to rupture the membranes before injecting the paste. It was extremely rare for shock to take place in connexion with these operations. He said that he did "quite a lot of this kind of work—more than the average gynaecologist."

Findings at Necropsy

Dr. Keith Simpson reported that at necropsy the most careful routine examination failed to reveal any evidence of organic disease of any kind. There was no deformity or disproportion of the pelvis likely to interfere with the normal termination of a full-term pregnancy. A seven-months gestation was present and in a healthy state, capable of continuation to term. The cervix had been dilated and a gelatinous paste introduced, separating the sac of the pregnancy for about an inch around the internal orifice of the neck of the womb. There was no pulmonary embolism and only the slightest bleeding had occurred. The entire absence of any organic cause of death

gave proper grounds for the inference that death was due to reflex shock. Shock would not reflect lack of skill in the procedure, but light anaesthesia in an emotional subject would predispose to it. In his opinion the cause of death was shock due to artificial abortion. It would have been perfectly easy to deliver this child alive by immediate operation on the apparent death of the mother. It was viable in law, having reached the 28th week, and his examination revealed no reason to suppose that it was not alive in the uterus.

Shock was a well-recognized possible consequence of either dilating the cervix or of injecting any substance into the uterus. Death in such cases was quite sudden, unheralded, and might ensue within a few seconds. He thought it was remotely possible, but unlikely, that death did not take place until ten minutes after the operation, as had been suggested by the matron. There was no evidence that what had been done had not been done skilfully. There were facilities in any general hospital for performing such operations if they were necessary. This could come under the National Health Service without cost to the family of the patient.

The jury returned a verdict of misadventure in accordance with the medical evidence and added a rider recording its opinion "that decisions to undertake operations of this type should be more strictly safeguarded, and such operations should be carried out only in State hospitals under the National Health Scheme."

Medical Notes in Parliament

LONDON CENTRE FOR TROPICAL MEDICINE

Mr. IVOR THOMAS on April 27 recalled how in 1898 Mr. Joseph Chamberlain, Sir Patrick Manson, and Sir Percival Nairne had founded at the Albert Dock Hospital the London School of Tropical Medicine. Manson's idea was that teaching, treatment, and research should be carried on by one organization in one group of buildings. When the first world war ended, the Hospital for Tropical Diseases was established in Gordon Street, and the school was reopened there in 1920. In 1924 the school was merged in the London School of Hygiene and Tropical Medicine. This separated teaching from the treatment of tropical diseases, but nevertheless Britain maintained a high place in both teaching and treatment until the outbreak of the second world war. The building in Gordon Street then had to be closed because it was unsuitable as a hospital under threat of air attack. A little later a land mine fell behind it. It then became necessary to consider what provision should be made after the war, and in April, 1941, Lord Moyne appointed an interdepartmental committee to go into the question. After the end of the war a temporary hospital was opened in Devonshire Street. Good work had been done there and the staff had rendered devoted service, but accommodation was very limited, and no one would claim that the hospital was an adequate centre. He thought there should be set up in London a comprehensive hospital for tropical diseases with the status of a postgraduate teaching hospital and with its own board of governors. It should be erected within the curtilage of the University of London to be close to the London School of Hygiene and Tropical Medicine. It would probably cost £1,000,000, but nothing short of such a scheme would meet the need.

Mr. Bevan had told him on Feb. 10 (*Journal*, Feb. 19, p. 328) that it was proposed to develop a tropical diseases centre as a unit of the University College Hospital group. What was wanted was a tropical diseases hospital with 150 beds and an outpatient department of the polyclinic type.

Dr. HADEN GUEST said Mr. Thomas was out of touch with the present difficulties in regard to staffing. Anything like the scheme Mr. Thomas suggested was out of the question at present.

Dr. STEPHEN TAYLOR said, as a comparatively recently appointed governor of University College Hospital, that the collection of tropical cases was a practical difficulty. Until recently places in the existing temporary hospital were nothing like filled. This was due in part to the fact that many medical officers and specialists had had experience in the Forces of the treatment of tropical diseases and were anxious to use that experience in treating cases in non-tropical disease hospitals and general wards in London. On behalf of the governors of University College Hospital he assured Mr. Thomas that their desire was to see a worthy tropical diseases hospital and unit developed as part of that hospital. The governors hoped the new location of the tropical diseases hospital would be in the old St. Pancras Hospital not much farther away from the University of London than the old building was.

Mr. BLENKINSOP, replying to the debate, said everybody desired proper provision in London for the treatment of tropical diseases and the teaching of tropical medicine. After the report of the interdepartmental committee had been submitted a decision was taken that instead of going forward on the line then suggested, which was out of keeping with the development of the National Health Service, it would be preferable not to develop a completely isolated and separate hospital but to have a separate unit in close association with one of the large teaching hospitals. In accordance with that decision the Devonshire Street Hospital had been associated with the University College Hospital group. It was true that the accommodation at Devonshire Street was too crowded, although some very good equipment was available and very valuable services had been given there. It was proposed to improve the facilities by adding a more adequate inoculation centre. The proposal now being considered by the University College Hospital group would provide a considerable unit distinct from but at the same time associated with St. Pancras. The suggestion was that a modern block could be utilized there which would have the facilities of a great hospital by its side. The Ministry hoped a decision would be reached on this soon. Quite properly University College Hospital must have regard to other factors. If this accommodation was used for tropical medicine other plans must be re-examined. But, after seeing both premises and meeting some of those concerned, Mr. Blenkinsop was satisfied that University College Hospital was as anxious as was the Ministry to ensure that proper facilities should be available as rapidly as possible. As it became possible to undertake larger building projects larger schemes could be undertaken. He thought the proposal under consideration would meet immediate needs adequately.

Beds Not in Use

Mr. BEVAN said on April 28, replying to Colonel STODDART-SCOTT, that the number of beds closed for want of staff in hospitals in Great Britain on Dec. 31, 1948, was 59,903, made up as follows:

Tuberculosis sanatoria	5,669
Fever hospitals	15,915
General hospitals	21,642
Other specialized institutions	16,677
	59,903

Colonel Stoddart-Scott further asked how much of the £15,000,000 required to staff and maintain these 60,000 hospital beds had been included in Mr. Bevan's estimates for the coming year.

Mr. Bevan said the annual budgets of the hospital management committees did not specify separately anticipated expenditure on the reopening of closed beds, so that he was unable to give the information desired.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

On April 23 the degrees of M.B., B.Chir., were conferred on Muri E. Sidaway.

A Pinsent–Darwin Studentship has been awarded to John McFi M.B., B.Chir.

A course in paediatrics and obstetrics will be held at Addenbrooke Hospital, Cambridge, from May 16 to 27. Eleven half-day sessions will consist of lectures and demonstrations. Details of the course the number attending which is limited, may be obtained from the secretary, the Medical School, the Naval Hut, Downing College Cambridge.

UNIVERSITY OF BIRMINGHAM

Professor E. B. Verney, F.R.S., Sheild Professor of Pharmacology in the University of Cambridge, will deliver the William Withering Lectures in the Anatomy Theatre of the Medical School of the University on May 12, 13, 16, and 17, at 4 p.m. His subject is "The Excretion of Water by the Kidney, with Special Reference to its Neurohypophysial Control."

The Ingleby Lectures will be delivered by Mr. Charles D. Read Director of Postgraduate Studies, Chelsea Hospital for Women, in the Anatomy Theatre of the Medical School of the University on May 19 and 26, at 4 p.m. His subject is "Some Problems of Stress Incontinence of Urine in the Female."

Members of the medical profession and students of medicine are invited to attend the lectures.

No. 15

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 16.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949					1948 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	27	2	8	2	—	47	3	15	3	2
Deaths		—	1				1	—		
Diphtheria	103	7	28	4	4	136	12	53	11	3
Deaths	1	—	1	—	—	2	1	—	—	1
Dysentery	49	7	16	—	3	110	30	47	—	—
Deaths		—		—	—		—		—	—
Encephalitis lethargica, acute	—	—	—	1	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			19	7	4			46	10	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				22					27	
Deaths	24	3	3	3	—	35	3	5	5	—
Measles*	13,066	1635	299	203	172	9,681	1360	315	96	45
Deaths†			—	—	—			2	1	—
Ophthalmia neonatorum	44	2	13	—	—	54	1	13	—	—
Deaths										
Paratyphoid fever	1	—	1(B)	—	—	7	—	1(A)	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	731	30	9	21	18	639	54	8	12	2
Deaths (from influenza)‡	95	6	2	2	—	10	—	2	1	1
Pneumonia, primary			202	43				213	30	
Deaths	277	36		10	9	205	45		9	8
Polio-encephalitis, acute	2	—				1	—			
Deaths										
Poliomyelitis, acute	5	2	1	—	—	19	1	2	1	—
Deaths§	—	—				3	—			
Puerperal fever		—	5				2	11		—
Deaths										
Puerperal pyrexia‖	81	9	3	2	1	114	4	8	6	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,039	65	162	73	36	1,290	76	252	37	38
Deaths†			—	—	—			—	—	—
Smallpox	7	3	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	2	—	—	—	—	9	—	—	2	—
Deaths	—	—	—	—	1	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,267	194	150	79	73	3,888	286	61	69	22
Deaths	11	3	1	3	1	13	2	1	—	—
Deaths (0–1 year) Infant mortality rate (per 1,000 live births)	335	38	30	27	8	338	53	44	25	12
Deaths (excluding still-births)	5,187	753	642	206	130	4,651	738	619	180	120
Annual death rate (per 1,000 persons living)			12·9	12·8				12·5	11·3	
Live births	6,880	1152	894	375	253	8,469	1366	1062	341	259
Annual rate per 1,000 persons living			17·9	23·2				21·4	21·3	
Stillbirths	180	27	22			211	30	31		
Rate per 1,000 total births (including stillborn)			24					28		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales, Eire, and Northern Ireland.

EPIDEMIOLOGICAL NOTES

Typhoid Fever at Crowthorne

The diagnosis of typhoid fever was confirmed on April 30 in a patient admitted to the Royal Berkshire Hospital from Crowthorne, which has a population of 3,500. During the next two days the diagnosis was confirmed in four other patients, and a total of 32 persons were suspected of suffering from the disease. The earliest of the dates of onset so far mentioned is April 21. The usual steps have been taken by way of prevention and control, but in any event an outbreak of considerable magnitude is to be expected. It cannot be assumed that the disease will remain confined to Crowthorne until the source and vehicle of infection have been identified.

Crowthorne is at the junction of the territory of three regional hospital boards: North-west Metropolitan, South-west Metropolitan, and Oxford. Cases are known to have been admitted to hospital at Winchester as well as at the Reading hospital. The organism has been identified as Vi-phage Type E1.

Smallpox

The last of the eleven cases of smallpox imported on the s.s. *Mooltan* was removed to hospital on April 16. The period of surveillance of the numerous contacts with these cases has now expired without notification of the disease in any of them. Although there is reason to hope that the infection has not passed to anyone in this country it is too early to exclude the possibility of a missed case, because at least one of the patients may have been in contact with persons who could not be brought under surveillance. Special vigilance should therefore continue for a further two or three weeks.

Fortunately the passengers and crew of the s.s. *Mooltan* gave the public health authorities helpful co-operation. The persons who developed the disease were removed early and before they could do much damage. With very few exceptions contacts accepted vaccination promptly and remained under surveillance. The several public health departments concerned, particularly those for the ten districts in which the imported cases were taken ill, appear to have carried out the routine measures for the control of smallpox without a hitch.

The patients who survived are now making satisfactory progress, and the case fatality, 6 out of 12, is unlikely to alter. In two patients modification by previous vaccination had reduced the disease to a triviality; variola virus was recovered, however, on egg culture. Virus was also recovered from the remaining cases except the one at Liverpool.

Future Population Trends

The birth rate during 1948 was 17.9 per 1,000 and 2.7 below the post-war peak of the preceding year. Except for 1946 and 1947, however, this rate was the highest since 1922. The rise in the birth rate following the war was apparently of a temporary nature and was not, as has been suggested, due to a permanent increase in the average size of families. The effective reproduction rate corresponding to the births which occurred in 1948, after making allowance for a continuing improvement in the likelihood of survival, has been provisionally assessed at 1.070. With present trends this rate will fall during the next year or so to below 1.0, which is the level of replacement. The marriage rate at 18.1 remained fairly high. From 1921 to 1937 this rate varied between 14.3 and 17.5. The maintenance of a high marriage rate means that the birth rate may remain above the level of the years immediately preceding the war.

A forecast by the Registrar-General, based on the present trends, suggests that in 1960 there will be 22.3% of the population under the age of 15 and 12.1% aged 65 and over, compared with 21.4% and 10.7% in 1948. The school population will be at its peak, and with the present trends a decline must be expected after this date. On the other hand the number of pensioners will continue to increase and become proportionately more important, placing a gradually increasing burden on the social services.

Notifications During First Quarter

In the first thirteen weeks of this year whooping-cough and acute pneumonia have been unusually prevalent, and so has measles. The fall in the incidence of diphtheria has continued, and the notifications were only one-quarter of the number recorded four years ago and about one-fourteenth of the number recorded in the first thirteen weeks of 1938. Notifications of dysentery and of cerebrospinal fever were the lowest of recent first quarters. The incidence of acute poliomyelitis showed a considerable improvement on the preceding year but remains above the pre-epidemic level. The number of deaths

attributed to influenza in the great towns was higher than in recent first quarters. The figures for the first quarters of the past five years were as follows:

England and Wales	1945	1946	1947	1948	1949
Scarlet fever ..	19,163	16,952	15,527	23,348	16,087
Whooping-cough ..	19,780	20,033	27,922	35,034	37,221
Diphtheria	6,061	6,220	2,832	2,466	1,523
Measles	247,455	17,652	165,895	88,489	201,140
Acute pneumonia ..	14,782	16,278	15,500	10,969	17,147
Cerebrospinal fever	968	906	1,110	629	479
Acute poliomyelitis	61	104	114	381	224
Dysentery	4,681	4,444	931	2,100	886
Enteric (typhoid and paratyphoid fevers)	140	138	98	103	100
Great Towns					
Influenza deaths ..	693	2,156	1,335	272	2,278

Discussion of Table

In *England and Wales* infectious diseases were less prevalent during the week, and there were decreases in the incidence of measles 1,658, whooping-cough 341, acute pneumonia 362, scarlet fever 152, and dysentery 14.

Large decreases in the notifications of measles were recorded in Southampton 213, Lancashire 150, Hertfordshire 138, London 118, and Essex 111; the chief exception to the general decline was an increase of 109 in Middlesex. There was a fall in the incidence of whooping-cough in every area except in London and the south-eastern counties, where an increase of 39 in the notifications was reported.

An outbreak of diphtheria affected 8 persons in Berkshire, Wokingham R.D., and there was an increase of 9 in the notifications in Staffordshire. A small decrease was recorded in the notifications of scarlet fever in most areas, the largest exceptions to the general trend being rises in Lancashire 15 and Yorkshire 11. A fall in the incidence of acute pneumonia was general throughout the country.

The chief centres of infection for dysentery were Lancashire 11 (Liverpool C.B. 8) and Yorkshire West Riding 13 (Huddersfield C.B. 11).

In *Scotland* there was a rise of 9 in the incidence of diphtheria, and there were falls in the notifications of measles 87, whooping-cough 72, scarlet fever 31, and acute primary pneumonia 31. Dysentery reappeared in Edinburgh, where 8 cases were notified during the week. In Glasgow the notifications of dysentery fell from 20 to 5.

In *Eire* decreases were recorded in the notifications of scarlet fever 35, whooping-cough 32, and diarrhoea and enteritis 21. These changes were mainly due to the experience of Dublin C.B.

In *Northern Ireland* decreases were reported in the notifications of whooping-cough 31 and measles 21. In contrast to the general trend, increases in the notifications of measles were reported from Belfast C.B. 10 and County Antrim 11.

Week Ending April 23

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 953, whooping-cough 2,546, diphtheria 95, measles 13,514, acute pneumonia 759, cerebrospinal fever 34, acute poliomyelitis 8, dysentery 52, smallpox 5, paratyphoid 7, and typhoid 3. Deaths from influenza in the great towns numbered 51.

The Services

DEATHS IN THE SERVICES

Surgeon-Lieutenant JOHN MICHAEL ALDERTON, R.N., was killed in action in H.M.S. *Amethyst* on April 20. Born at Colchester on Oct. 19, 1924, he came of a medical family, his father, grandfather, and great-uncle all being members of the medical profession. He was educated at Epsom College, having gained the Leverhulme Scholarship there in 1938. On leaving Epsom he won a scholarship at University College Hospital, London. After graduating M.B., B.S. in 1946, he held the post of casualty officer at the British Postgraduate Medical School, Hammersmith. John Alderton was commissioned in the Royal Navy in September, 1947, and sailed for Hong Kong to join H.M.S. *Amethyst* in the following January. Outside medicine his two main interests were music and yachting. He was a keen member of the United Hospitals Sailing Club. He also played hockey for University College. He was of a naturally shy disposition but had a lovable character and keen sense of humour. All who knew him well will not be surprised that he merited the high tribute paid to him by the Admiralty: "He moved round the ship unflinchingly, aiding the wounded until he himself was killed." Our sympathy goes out to his parents and younger brother.—M.H.C.

Medical News

Dr. Douglas Fairley

Dr. Douglas Fairley has been appointed a Nominated Member of the Executive Council of the Island of St. Helena.

Dr. John Gillies

Dr. John Gillies, one of the doctors in attendance on the King at his recent operation, has been appointed a Commander of the Royal Victorian Order.

Spectrographic Research Unit

By arrangement with the London Hospital, the Medical Research Council has established there a Spectrographic Research Unit under the direction of Dr. E. R. Holiday. The primary function of the unit is to undertake original research work in the field of absorption spectrophotometry as applied to biological problems of medical interest, but advice and assistance will also be given to other branches of the Council's organization using such methods. The unit has been based on the spectrographic department originally established by the London Hospital, and during the last five years partly supported by the Council for the purposes which are now being developed.

Invitation from Professor C. R. Marshall

An invitation is extended to all members of the class of materia medica at Aberdeen University from 1919 to 1930 inclusive who are attending the B.M.A. Meeting in Harrogate to a dinner at the Troutbeck Hotel, Ilkley, on Friday, July 1, at 7 p.m. Buses from Harrogate will be provided. Those wishing to accept should write, saying if accompanied by a lady, to Professor Marshall, Annisholme, Manor Park, Burley-in-Wharfedale, Yorkshire, before June 7.

Lecturing in Italy

Dr. Margaret Tod, Deputy Director of the Holt Radium Institute, Manchester, is visiting Italy between May 5 and 21 to meet Italian radiotherapists in preparation for the International Radiological Congress to be held in England in 1950. She will also lecture for the British Council in Milan, Bologna, Florence, and Rome on "Cancer Organization and Our Clinic System" and "Accurate Dosage in Radium and *X*-ray Therapy."

Royal Commission on Capital Punishment

Dr. Eliot Slater has been appointed a member of the Royal Commission on Capital Punishment. The following are the other members: Sir Ernest Gowers (chairman), Mrs. E. D. C. Cameron, Mr. N. R. Fox-Andrews, K.C., Miss Florence Hancock, Mr. William Jones, Mr. Horace Macdonald, Mr. John Mann, Sir Alexander Maxwell, Professor G. A. Montgomery, K.C., Lord Peel, Professor Leon Radzinowicz. The secretary is Mr. F. L. T. Graham-Harrison, of the Home Office. The terms of reference of the commission are: To consider and report whether liability under the criminal law in Great Britain to suffer capital punishment for murder should be limited or modified, and, if so, to what extent and by what means; for how long and under what conditions persons who would otherwise have been liable to suffer capital punishment should be detained, and what changes in the existing law and the prison system would be required; and to inquire into and take account of the position in those countries whose experience and practice may throw light on these questions. Those wishing to give evidence should apply to the secretary, submitting a written statement of the evidence which they wish to give. Communications should be addressed for the present to the secretary, Royal Commission on Capital Punishment, Home Office, Whitehall, London, S.W.1.

Control of Tropical Diseases

In accordance with proposals agreed to by the Economic Co-operation Administration in Washington to aid development of certain areas in the British Empire, Dr. Frederick J. Brady, of the U.S. Public Health Service, and Mr. Harry H. Stage, of the U.S. Department of Agriculture, will visit Africa to study the control of trypanosomiasis and malaria. They will leave New York on May 10, and after consulting the Colonial Office in London will visit East and West Africa, will survey the conditions there, and make recommendations on further U.S. assistance in combating the tsetse fly and mosquito.

Aftercare of Delinquents

The Home Secretary has approved the establishment of a Central Aftercare Association for England and Wales to supervise persons released from Borstal training, corrective training, and preventive detention, and young prisoners released on licence. The Borstal Association, the Aylesbury Aftercare Association, and the Central Association for the Aid of Discharged Convicts are to be merged in it.

Streptomycin under Marshall Aid

The Economic Co-operation Administration has stated that streptomycin to the value of £2,500,000 has been provided under Marshall Aid for the treatment of tuberculosis in Europe. E.C.A. funds are also financing the reconstruction of two French plants to produce the drug.

Soap for Bedridden Patients

On the recommendation of his medical advisers the Minister of Food has decided that bedridden patients who suffer also from a condition for which extra soap is granted may receive both the special allowance of soap appropriate to their condition and the one extra ration of soap to which they are entitled because they are bedridden. Doctors are asked, when authorizing extra soap for their bedridden patients, to write the word "bedridden" on the R.G.50 and not quote the classification of this condition in MED.2 (Revised 1948). If a bedridden patient also qualifies for soap under another classification in the MED.2 (Revised 1948), that classification should be quoted and the word "bedridden" added to it, so that extra soap can be made available to the patient on both counts. Patients whose condition requires the liberal application of ointments, pastes, or similar preparations qualify for one extra soap ration a week. They must present at the Local Food Office a medical certificate stating that soap is required for that reason.

Director of Army Health

The title of Director of Hygiene at the War Office has been changed to Director of Army Health. The titles of Deputy Directors, Assistant Directors, and Deputy Assistant Directors have been changed similarly. Specialists in Hygiene are now entitled Specialists in Army Health. The present Director of Army Health is Brigadier A. E. Richmond.

Association of Independent Hospitals

The independent hospitals and kindred organizations—by which is meant hospitals, convalescent homes, epileptic colonies, and other institutions that have either been disclaimed from, or were not transferable under the Acts to, the National Health Service—have formed an Association of Independent Hospitals and kindred organizations. Its objects are to safeguard and develop the interests of these hospitals, which are the remaining voluntary hospitals of the country and therefore are wholly dependent on the public and on themselves for maintenance.

Peruvian Academy Honours Medical Historian

At a special meeting of the Peruvian Academy of Surgery held in Lima on Feb. 11 Dr. Douglas Guthrie, lecturer on the history of medicine in the University of Edinburgh, who has been acting as visiting professor to the University of San Marcos, was admitted to the honorary membership of the Academy. Dr. Guthrie is the first British surgeon to receive this distinction, which was accompanied by the presentation of an enamel badge bearing the emblem of the Academy, the spade-shaped knife or "tumi" which was used by the Incas for their primitive trephining operations.

World Federation for Mental Health

The first number of the *Bulletin* of the World Federation for Mental Health has been issued as a successor to the series of twelve bulletins distributed by the International Congress on Mental Health held in London last year. The *Bulletin* is intended to serve as a link between the Federation and member associations in different countries. It is also intended for the exchange of ideas and information on the principles and practice of mental health throughout the world. In each issue it is proposed to publish at least one original article on some topic relevant to the Federation's work. It may be obtained for 5s. a year (post free) from the editor, at the World Federation for Mental Health, 19, Manchester Street, London, W.1.

Blockaded Berlin

An official pamphlet, *Notes on the Blockade of Berlin, 1948*, touches on the public health problems of the blockaded area. So far 8,652 undernourished children have been flown out to the Western Zones by the British air lift. The first medical supply to be flown in was ether, which had formerly come from the Eastern Zone. A number of patients have been removed from hospitals to the Western Zones so that the beds in Berlin may be used so far as possible for cases of serious or acute sickness. The chief types of cases evacuated are those requiring specialized treatment unavailable in Berlin or a long rest and good food, and cases of early and ambulatory tuberculosis and of convalescent poliomyelitis.

Recognition for War Service

The President of the Czechoslovak Republic has conferred the decoration of Chevalier of the Order of the White Lion upon Drs. Hector Macdonald Walker, O.B.E., and Thomas Forrest Cotton in recognition of services rendered during the war.

Aberdeen Children's Welfare Council

At a recent conference at Aberdeen of organizations whose principal objects include the care of children it was decided to form a Children's Welfare Council. It will help to correlate the work of the various bodies concerned with child care in all its social aspects. Professor John Craig, of the Department of Child Health, Aberdeen University, is chairman, and Mr. Auld, of the Association of Social Service, is secretary.

Wills

Dr. Theodore Shennan, Regius Professor of Pathology at Aberdeen University 1914–36, left £4,561. Dr. Herbert John Pulling, of Brighton, left £37,909; Dr. Archibald Deane, formerly of Eastbourne, £18,907; Dr. Frederick Henry Healey, formerly medical superintendent of Hellesden Mental Hospital, £4,226; and Lieut.-Col. Henry Smith, late I.M.S., £57,240.

COMING EVENTS

Royal Society Lectures

The Bakerian Lecture for 1949 will be delivered on May 12 by Professor H. Raistrick, F.R.S., Professor of Biochemistry at London University. The Croonian Lecture for 1949 will be delivered on June 30 by Dr. D. W. Bronk, Foreign Member of the Royal Society. Dr. Bronk is Foreign Secretary of the National Academy of Sciences and Chairman of the National Research Council of the U.S.A. The Wilkins Lecture for 1949 will be delivered on Dec. 15 by Professor E. N. da C. Andrade, F.R.S., Quain Professor of Physics at London University.

National Industrial Safety Congress

The Royal Society for the Prevention of Accidents will hold the National Industrial Safety Congress on May 13–15 at Scarborough. It is open to non-members as well as members. Speakers include Sir Geoffrey King, Deputy Secretary at the Ministry of National Insurance, and Sir Charles Bartlett, managing director of Vauxhall Motors Limited. Particulars may be obtained from the Industrial Safety Division of the Royal Society for the Prevention of Accidents, 131, Sloane Street, London, S.W.1.

Lectures on Psychology

The Institute for the Scientific Treatment of Delinquency has arranged a course of eight lectures on "Selected Topics in Psychology" to be given by Miss Gertrude Keir, M.A., at the Institute, 8, Bourdon Street, Davies Street, London, W., on Thursdays, commencing May 26, at 6.30 p.m. The lectures are intended for students who have some basic knowledge of elementary psychology, and the fee for the course is 10s. Those wishing to attend should make early application to the Education Secretary.

Charities Ball

A Charities Ball organized by the Metropolitan Counties Branch of the B.M.A. will be held at B.M.A. House, Tavistock Square, London, W.C.1, on Thursday, May 26, at 8 p.m. for 8.30 p.m. The proceeds will be devoted to medical charities in urgent need of support. Patrons include the President of the Association and the Presidents of the three Royal Colleges. There will also be a cabaret and facilities for bridge. The cost of tickets including a buffet supper is two guineas each. Applications should be sent to the Secretary, the Charities Ball Committee, Metropolitan Counties Branch, B.M.A. House. Contributions to charities from those unable to attend the ball would also be most welcome and should be sent to the same address.

Tuberculosis Meeting at Liverpool

A joint meeting of the British Tuberculosis Association and the North-Western Tuberculosis Society will be held at the Medical Institution, Mount Pleasant, Liverpool, on Friday and Saturday, May 27 and 28. The programme is as follows: May 27, 2 p.m., Sir Henry Cohen, "Tuberculosis and General Medicine"; 2.45 p.m., discussion on "Domiciliary Treatment of Pulmonary Tuberculosis," to be opened by a representative of the British Tuberculosis Association, followed by Dr. R. Heller and Dr. C. H. C. Toussaint; 4.45 p.m., discussion on "Tuberculosis in Seamen," to be opened by Dr. R. N. Walker; 5.45 p.m., extraordinary meeting of British Tuberculosis Association; 7.30 for 8 p.m., informal dinner at Reece's Restaurant, Parker Street, Liverpool. May 28, 9 a.m., general meeting of British Tuberculosis Association; 9.15 a.m., demonstration of a series of cases of pulmonary tuberculosis treated by the more recent developments of surgery, as follows: "Thoracoplastic Operation using the Polythene Pack," by Mr. H. Morriston Davies and Mr. Leslie J. Temple, and (1) "Periosteo-plastic Pneumonolysis" and (2) "Lung Resection," by Mr. F. Ronald Edwards; 10.45 a.m., "Rehabilitation in Surgical Tuberculosis," by Mr. J. P. Heron; 12 noon, colour film, "Surgical Treatment of Tuberculous Epididymitis" (by courtesy of Mr. J. Cosbie Ross).

SOCIETIES AND LECTURES

Monday

EDINBURGH UNIVERSITY.—At Physiology Lecture Theatre, University New Buildings, Teviot Place, Edinburgh, May 9, 5 p.m., "*The Prehistory of Medicine*," by Dr. Douglas Guthrie.

LONDON: UNIVERSITY COLLEGE.—At Physiology Theatre, Gower Street, W.C., May 9, 4.45 p.m., "*Selective Toxicity with Special Reference to Chemotherapy*," by Professor Adrien Albert.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—May 9, 8 p.m., annual general meeting; 8.30 p.m., "*Temperament*," Annual Oration by Mr. A. C. Palmer.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal Society of Medicine, 1, Wimpole Street, London, W., May 9, 8.30 p.m., Cavendish Lecture: "*The Contribution of Law to Literature*," by The Rt. Hon. Mr. Justice Birkett.

Tuesday

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, Queen's Gate Terrace, London, S.W., May 10, 7 for 7.30 p.m. Annual dinner.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 10, 5 p.m., "*The Sclerodermas*," by Dr. C. B. Dowling.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—May 10, 2.15 p.m., "*The Respiratory Tract in Infectious Diseases*," by Dr. E. H. R. Harries.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., May 10, (1) 11 a.m., "*Serological Tests in the Diagnosis of Syphilis*," by Dr. R. Thomson; (2) 5 p.m., "*Genito-urinary Tuberculosis, I*," by Mr. F. J. F. Barrington.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., May 10, 5.30 p.m., "*Some Advances in Chemotherapeutic Research at the Pasteur Institute*," by Professor Jacques Tréfouël (Pasteur Institute, Paris).

LONDON: UNIVERSITY COLLEGE.—At Physiology Theatre, Gower Street, W.C., May 10, 5.15 p.m., "*Physiological Properties of Ethyl Alcohol*," by Dr. M. Grace Eggleton.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, Paddington, W.—May 10, 5 p.m., "*Biochemical Properties of the Bacterial Cell Wall*," by Dr. E. F. Gale.

Wednesday

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—May 11, 8 p.m., "*Pupillary Movements*," by Dr. Fergus Campbell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., May 11, (1) 11 a.m., "*Biological False-positive Reactions for Syphilis*," by Dr. R. Thomson; (2) 5 p.m., "*Calculous Disease of the Kidney and Ureter, I*," by Mr. H. P. Winsbury-White.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, Wandsworth Common, S.W., May 11, 8.30 p.m. Seventh meeting of session in conjunction with Wandsworth Division of B.M.A. Subject: Demonstration of cases by the honorary medical staff of Bolingbroke Hospital.

Thursday

BIRMINGHAM UNIVERSITY.—At Anatomy Theatre, Medical School, Birmingham, May 12, 4 p.m., "*The Excretion of Water by the Kidney, with Special Reference to its Neurohypophysial Control*," William Withering Lecture by Professor E. B. Verney, F.R.S.

DURHAM UNIVERSITY.—At Royal Victoria Infirmary, Newcastle-upon-Tyne, May 12, 5.15 p.m., "*The Morison Approach to Hydatid Disease*." Fifth Rutherford Morison Lecture by Professor C. F. M. Saint (Capetown).

EDINBURGH UNIVERSITY.—At Anatomy Theatre, University New Buildings, Teviot Place, May 12, 5 p.m., "*Medical Aspects of Splenectomy*," Honyman Gillespie Lecture by Dr. H. N. Robson.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 12, 5 p.m., "*Anogenital Pruritus*," by Dr. B. Russell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., May 12, (1) 11 a.m., "*Congenital Syphilis*," by Dr. S. M. Laird; (2) 5 p.m., "*Genito-urinary Tuberculosis, II*," by Mr. F. J. F. Barrington.

ROYAL SOCIETY, Burlington House, Piccadilly, London, W.—May 12, 4.30 p.m., "*A Region of Biosynthesis*," Bakerian Lecture by Professor Harold Raistrick, F.R.S.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—May 12, 4.30 p.m., "*Psychiatry*," lecture-demonstration by Dr. D. Curran.

Friday

BIRMINGHAM UNIVERSITY.—At Anatomy Theatre, Medical School, Birmingham, May 13, 4 p.m., "*The Excretion of Water by the Kidney, with Special Reference to its Neurohypophysial Control*," William Withering Lecture by Professor E. B. Verney, F.R.S.

LONDON UNIVERSITY.—At King's College, Strand, W.C., May 13, 5.30 p.m., "*Heart Metabolism and Coronary Disease*," by Professor Kl. Gollwitzer-Meier (Hamburg).

ROYAL MEDICAL BENEVOLENT FUND.—At Medical Society of London, 11, Chandos Street, Cavendish Square, W., May 13, 5.15 p.m., 113th general meeting.

Saturday

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Royal Sea Bathing Hospital, Margate, May 14, clinical session, presided over by Dr. B. W. Armstrong, followed by luncheon at Nayland Rock Hotel, Margate.

APPOINTMENTS

MIDDLEMISS, J. H., M.D., D.M.R.D., F.F.R., Director of Radiodiagnostic Department, United Bristol Hospitals.

Dr. Middlemiss graduated at Durham University in 1940 and proceeded M.D. in 1947. He was formerly Assistant Radiologist at the Royal Victoria Infirmary, Newcastle-upon-Tyne, and is the author of several papers on radiodiagnosis.

Dr. James A. Doull, Medical Director, U.S. Public Health Service, has been appointed Medical Director of the Leonard Wood Memorial (American Leprosy Foundation). Dr. Doull succeeds Dr. H. Windsor Wade, who, because of ill health, has been relieved of administrative duties and appointed associate medical director. Dr. Wade will continue his pathological studies at Culion, Philippine Islands, and the editorship of the *International Journal of Leprosy*. The headquarters of the medical department of the Memorial has been transferred from Culion, P.I., to 1832 M Street, N.W., Washington 6, D.C., U.S.A.

BAIRD, MISS EBA CRICHTON, M.B., Ch.B., D.P.H., Assistant Medical Officer, Burgh of Hamilton, Lanarkshire.

FAY, LEO, M.D., D.P.H., Deputy County Medical Officer, Somerset County Council.

LAWSON, T. O. P. D., M.B., Ch.B., D.Obst.R.C.O.G., D.P.H., Medical Officer of Health and School Medical Officer, County Borough of Dudley.

PARKER, W. S., M.B., Ch.B., D.P.H., D.I.H., Deputy Medical Officer of Health, County Borough of Brighton.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Armin.—On April 18, 1949, to Dr. Margaret Armin (née Conway), wife of Dr. Richard Armin, a third daughter.

Brownlee.—On April 1, 1949, at Edinburgh, to Margot, wife of T. J. Brownlee, F.R.C.S.Ed., twin sons.

Glanvill.—On April 10, 1949, at Maternity Wing, General Hospital, Sunderland, to Dr. Catherine Glanvill, wife of Dr. Terry Glanvill, a daughter.

Green.—On April 25, 1949, to Drs. Mildred and Norman Green, of Stoke-on-Trent, a son.

Rigby.—On April 19, 1949, at Lewisham, to Joan, wife of Dr. J. P. V. Rigby, a daughter.

Woodruff.—On April 25, 1949, at the Middlesex Hospital, London, W., to Helen, wife of Dr. A. Waller Woodruff, a daughter.

Yeates.—On April 3, 1949, at Newcastle-upon-Tyne, to Mr. and Mrs. W. Keith Yeates, a daughter.

MARRIAGES

Gordon—Harris-Wright.—On April 23, 1949, at St. George's, Hanover Square, London, W., Ian James Gordon, M.B., Ch.B., Aberdeen, to Pamela Nonette Harris-Wright, M.B., B.S., M.R.C.S., L.R.C.P., London.

Thomson—Mowat.—On April 14, 1949, at Heath Congregational Church, Halifax, George William Rosslyn Thomson, M.B., B.S., to Mary Stewart Mowat, M.B., Ch.B.

DEATHS

Barclay.—On April 26, 1949, at Oxford, Alfred Ernest Barclay, O.B.E., M.D., D.Sc., F.R.C.P., of Oxford and Manchester.

Churchill.—On April 23, 1949, Joseph Henry Churchill, M.R.C.S., L.R.C.P., of Byland House, Cleveland Walk, Bath.

Delva.—On April 21, 1949, at Fielden House, London Hospital, Joseph Delva, M.D., of Hatherley House, Central Park Road, East Ham, E.6.

Halliday.—On April 18, 1949, at Highlands, Lacey Green, near Princes Risborough, Bucks, John Rutherford Halliday, M.D.

Hocken.—On April 16, 1949, at 8, Tremena Road, St. Austell, Cornwall, Melville Hocken, M.B., B.S., formerly of Halesworth, Suffolk.

Hodson.—On April 18, 1949, at his home, Snaresbrook, Bergholt Road, Colchester, Essex, Howard Bluntisham Hodson, M.D., D.P.H., aged 42.

McKettrick.—On April 14, 1949, Frederick John McKettrick, M.B., C.M.Ed., of Dane View, Danbury, Chelmsford, Essex, aged 84.

Melville.—On April 14, 1949, at Millbank Military Hospital, London, S.W.1, very suddenly, Charles William Francis Melville, C.B., M.B., Ch.B.Ed., Major-General I.M.S., Ret., aged 72.

Neilson.—On April 13, 1949, at Woking, Surrey, Henry John Neilson, C.B.E., M.D., aged 86.

Pattison.—On April 9, 1949, at 39, Montpellier Villas, Cheltenham, Blanche Sutton Pattison, M.R.C.S., L.R.C.P., aged 52.

Pawson.—On April 12, 1949, at Dyserth, Flintshire, Edward Basil Pawson, M.B., B.Chir.

Peach.—On April 5, 1949, at Palmerston North, New Zealand, Charles William Peach, M.B., C.M., aged 76.

Richards.—On April 18, 1949, at Downes, Monkleigh, Bideford, Devon, Owen William Richards, C.M.G., D.S.O., M.Ch., F.R.C.S.

Sewell.—On March 13, 1949, Sir Sidney Valentine Sewell, M.D., F.R.C.P., F.R.A.C.P., of Victoria, Australia.

Syme.—On April 14, 1949, at Barnellan, Bardowie, Stirlingshire, William Smith Syme, M.C., M.B., Ch.B., F.R.F.P.S.Glas.

Turner.—On April 17, 1949 (Easter Day), at Ty Newydd, Ruabon, North Wales, Annie Catharine (née Lyon), the faithful and beloved wife of Dr. A. H. Turner, and mother of Arthur and Isabel.

Warner.—On April 20, 1949, at Royal Devon and Exeter Hospital, Harold Percy Warner, M.B., B.S., of Rydal, Woodford Green, Essex, aged 63.

Wills.—On holiday at St. Helier, Jersey, James Robertson Wills, M.B., B.Ch., aged 46.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

First Aid for Carbolic Poisoning

Q.—*What first-aid treatment should be given in cases of poisoning by phenol and by cresol antiseptics?*

A.—The object of first-aid treatment in poisoning by phenol or related antiseptics must be to evacuate from the stomach as much of the ingested poison as possible and so prevent or minimize its absorption and its local effects. The main form of first-aid treatment is therefore gastric lavage. Repeated large quantities of lukewarm water should be used until the washings are free from the smell of carbolic. This end-point may be difficult to determine, as the operator, often working in an atmosphere laden with the smell of carbolic, will fail to detect by smell the relatively faint traces of the substance in the later washings. After this repeated lavage one of the reputed antidotes may be introduced into the stomach—for example, magnesium sulphate or sodium sulphate, 1 oz. (31 g.), or sugar of lime, ½ oz. (15.5 g.), in half a pint (284 ml.) of lukewarm water. The value of these substances is not satisfactorily established, however, and in any case they should be removed from the stomach after an interval of 10 to 15 minutes, and renewed if considered advisable. Alternatively, white of egg in milk may be administered, or liquid paraffin, either of which may be of some use in diminishing absorption and protecting the alimentary mucosa. If the respiration is failing, artificial respiration should be maintained and respiratory and cardiac stimulants can be injected. Caffeine and fluids may be given by rectum. The administration of fluids intravenously is of value but can hardly be considered a first-aid measure.

It must be emphasized, however, that the feature of first-aid treatment most likely to be of substantial value is the prompt evacuation of the poison before absorption and severe local necrosis have taken place. Too much must not be expected from the routine use of any known antidote. It should be remembered that carbolic is absorbed through the skin and also by inhalation. Where the skin surface has been contaminated the area should be thoroughly cleansed, and for this purpose alcohol is recommended.

Intravenous Saline in Intermittent Claudication

Q.—*What is the rationale of the use of intravenous hypertonic saline in cases of intermittent claudication? Has this method of treatment proved of any value in cases with arteriosclerotic changes?*

A.—Intravenous injections of hypertonic saline have been used widely in the treatment of intermittent claudication, whether due to thrombo-angiitis or to arterial degeneration. Temporary benefit has often been reported. The effect is thought to be produced by suddenly increasing the blood volume and thus promoting vasodilatation, which favours the collateral circulation in the affected limb. The results obtained with saline are transient, and the method has fallen into disuse because it was often necessary to infuse a litre daily. Promising results were reported with plasma transfusion, but enthusiasm was damped when several patients developed homologous serum jaundice.

Serological Diagnosis of Whooping-cough

Q.—*To what extent can the serological diagnosis of whooping-cough be relied on? What recorded experiences are there bearing on this subject?*

A.—Various methods have been used to demonstrate the presence of specific antibodies in the blood of patients with whooping-cough. These antibodies develop rather late in the course of the infection, usually from the third week onwards, and are therefore of little value for early diagnosis. The two methods which have been most commonly used in this country are the complement-fixation test and the agglutination reaction. In a child a positive reaction to the complement-fixation test in a dilution of 1 in 4 or more of the patient's serum, using a killed culture of *Haemophilus pertussis* as antigen, is very suggestive of infection. The agglutination reaction is more variable and requires a fresh living culture for its performance. In the U.S.A. the opsonocytophagic reaction and a mouse test for protective antibody are also used. British references to the use of the complement-fixation test and agglutination reaction in pertussis are, respectively, Donald, A. B., *British Medical Journal*, 1938, **2**, 613; and Evans, D. G., and Maitland, H. B., *J. Path. Bact.*, 1939, **48**, 468.

Teaching Writing to the Left-handed

Q.—*Is there any standard method of teaching writing to the left-handed child? I know that such children should not be forced to use the other hand for writing, as this may lead to stammering or other forms of hesitancy.*

A.—In teaching left-handed children to write, the following method has been found useful: (1) Place the paper slanting to right, not left. (2) Hold the pencil 1½ to 2 inches (3.75 to 5 cm.) from the point, so that the hand does not block the view of what is being written. (3) Train the child to visualize beforehand what he is going to produce, as he would if drawing an object. (4) To encourage the movement from left to right, start by using both hands at the same time, making circles and strokes. Practise slope towards right. (5) Write from a copy, very slowly and carefully, beginning with repeated single letters and without lifting the pencil from the paper. (6) Develop ambidexterity in other skills, such as woodwork and games.

It is very important to avoid fatigue and hurry. Exercises should be carried out slowly and for short periods. The mechanical difficulties of left-handers are sometimes made worse by the anxiety of feeling an oddity, so this should of course be avoided so far as possible. It may be useful to stress the fact that the left-handed cricketer or tennis-player may confound his opponents by his sinister dominance.

Burning Buddleia

Q.—*When old Buddleia wood was burned in the garden I noticed a sweetish smell in the air and was affected in the nose and chest (I am a hay-fever subject). Not only did I sneeze, but I was rendered heavy and drowsy and "queer in the head." What particular ethereal oils or alkaloids in the tree would cause these reactions?*

A.—Hypersensitivity to odours of plant origin has often been recorded as a cause of asthma and rhinitis. Thus asthma may occur in carpenters working with the wood of coniferous and other trees. With regard to *Buddleia*, however, no record can be found in the standard botanical reference books of any ethereal oil or alkaloid occurring in any species growing in this country. A Mexican species—*Buddleia perfoliata*—has leaves which contain an oil with a peculiar but pleasant odour, due apparently to the presence of fatty aldehydes. This species, so far as is known, is not in cultivation in this country.

Weight Increase in Pregnancy

Q.—*What is the normal gain in weight of a pregnant woman, and what are the limits of normal variation? How is the increase accounted for?*

A.—The gain in weight during normal pregnancy is subject to wide variation, but for practical purposes is generally reckoned as 24 ± 10 lb. (10.9 ± 4.5 kg.). According to L. G. Chesley (*Amer. J. Obstet. Gynec.*, 1944, **48**, 563) two-thirds of normal women gain between 13 and 35 lb. (5.9 and 15.9 kg.) but one-sixth more than 35 lb. The total increase in any one case, however, is to some extent dependent on the woman's initial bulk, and Stander, H. J., and Pastore, J. B. (ibid, 1940, **39**, 928), suggest that it should not exceed 25% of the pre-pregnancy weight. There are, however, many exceptions even to this. The gain does not take place regularly throughout pregnancy. In the first three months there is often little change, and even a loss may be recorded, especially when the woman has vomiting or anorexia. In the last two or three weeks there is also a tendency to lose, or to cease to gain, weight, probably as a result of increased fluid excretion. It has been said that at no time should the monthly increase exceed 5 lb. (2.26 kg.), otherwise

it may indicate occult oedema and the threatened onset of toxaemia. In fact this sign is quite unreliable, and there may be a gain of as much as 10 lb. (4.5 kg.) in any one month without the development of toxaemia.

The increase in weight is accounted for by: full-term child, 7½ lb. (3.4 kg.); liquor amnii, 2½ lb. (1.1 kg.); placenta, 1 lb. (0.45 kg.); enlargement of uterus, 2 lb. (0.9 kg.); breast development, 3½ lb. (1.58 kg.); protein retention not included under other items, 4 lb. (1.8 kg.); increase in blood volume, 3½ lb. (1.58 kg.); while the remainder is due to fluid retention in the tissues and a general deposition of fat.

Sterilizing Skin before Injection

Q.—*What do you consider the best method of sterilizing the skin before immunization?*

A.—For sterilization of the skin before subcutaneous or intramuscular injection of antitoxin, toxoid, or vaccine used in passive or active immunization a quickly acting disinfectant is needed, and preferably one which stains the skin so that the sterilized area can readily be seen. For this purpose tincture of iodine, or 1 to 2% iodine in 70% alcohol, is undoubtedly the most effective, since it sterilizes the skin in the least time it takes to dry—about 15 to 20 seconds. The skin should not be previously washed. Alternatively, 70 to 80% alcohol by itself may be used; absolute alcohol and methylated spirit are much less effective. Some cationic detergent preparations like "cetavlon" or "zephiran" are also quickly effective if used in 70% alcohol. The mercurial preparations, antiseptic dyes, hypochlorite, ether, and "dettol" have a slower or otherwise imperfect disinfecting action on the skin.

Hyoscine Hydrobromide for a Child

Q.—*Is it safe to give hyoscine hydrobromide to a child of 23 months? If so, in what dosage? The child in question is always travel-sick, and is shortly going to Ireland.*

A.—It would be quite safe to give hyoscine hydrobromide to a child of 23 months. A suitable dosage would be 1/400 gr. (0.16 mg.) half an hour before sailing, and a second 1/400 gr. at sailing time.

Disturbed Micturition in Disseminated Sclerosis

Q.—*Can you suggest any treatment to counteract precipitancy and frequency of micturition in a case of disseminated sclerosis?*

A.—The precipitancy and frequency of micturition in disseminated sclerosis arise, of course, from interference with the pathways concerned with the higher control of the bladder reflexes. As the cause is the actual damage to or loss of these fibres, medical treatment is of necessity disappointing. Theoretically, decrease in sensation of the bladder will improve the complaint, but this is difficult to attain, and the nearest approach to it is the use of sedatives, which the patient has probably already tried. Any infection, ill-health, or deterioration in general well-being makes these symptoms worse, and therefore should be prevented if at all possible. Limitation of fluid intake within reasonable limits also helps. Atropine has been used, but is disappointing.

Toxicity of Phenobarbitone

Q.—*I am interested in the toxic reactions to phenobarbitone (soluble). What symptoms have been reported so far? What effect, if any, has it on the appetite?*

A.—Most of the reported cases of phenobarbitone poisoning by ordinary doses have occurred in people who have an idiosyncrasy to the drug. The most frequent symptoms have been various types of skin eruptions, often accompanied by fever, mental disturbances, and sometimes nausea, gastric pain, and diarrhoea. There is much variation in the central nervous symptoms, which include delayed effects, extreme depression, excitement, and sometimes even mania. As with alcohol, there is a certain amount of habituation, but little real tolerance develops, and withdrawal reactions characteristic of morphine have not been observed. Prolonged use may lead to the development of psychical degeneration and nausea.

Its effect on appetite has been studied only in rats (M. R. Jones, *J. comp. Psychol.*, 1943, **35**, 1). In these experiments each rat received 80 mg. per kilo of body weight daily, which is large by human standards. During the first week the drugged rats ate more than the control animals; after the first week they ate less. Cessation of injections after the sixth week caused a drop in the food intake in the experimental but not in the control groups. This decrease in food intake may be permanent, for the lower rate of growth persists.

Treatment of Gout

Q.—*What treatment is likely to benefit an active man aged 60 who has suffered for years from rheumatism and had his first attack of gout in the left big toe eight weeks ago? He has lived for some years in a hotel, and any request for a special diet, or any serious disability, would almost certainly result in his being asked to leave.*

A.—The presumption in this case appears to be that all the patient's previous "rheumatism" has in fact been due to latent gout, which has at last declared itself in its true colours. With regard to treatment, this of course implies a permanent regimen, although this need not be made unduly difficult in this case, for the reasons given. The patient should, however, avoid alcohol, lead as quiet and regular a life as possible, with early bed, and feed on simple, plainly cooked food without condiments. He should endeavour to avoid "offal," such as liver, heart, kidney, etc., and should considerably increase his intake of non-alcoholic fluids, preferably between meals. If in the future he has an acute attack, it will be essential to put him to bed for a day or two. Even if it is possible for him to struggle along, it is more likely to become chronic if he does so. For one day he should be given cinchophen 7½ gr. (0.5 g.) thrice daily. During this period he should also start taking tab. colchicin. 1/64 gr. (1 mg.) hourly until he develops slight diarrhoea or vomiting; he should then drop the colchicine to one tablet thrice daily for two weeks. In the intervals between the acute attacks, as regards medicinal treatment (provided there is no contraindication, such as liver disease), he should continue one day every month (say, Sunday) on cinchophen for the next six months; if the cycle can thus be broken, he may then develop no further acute attacks.

NOTES AND COMMENTS

Spread of Tuberculosis by Books.—Dr. T. PEIRSON (Plymouth) writes: With reference to the question and answer on the possibility of books handled by tuberculous patients carrying tubercle bacilli ("Any Questions?" April 2, p. 601), I was surprised to see the statement made in your answer: "Fortunately the bacilli become non-viable in about 48 hours when they are dry. . . ." Surely this is not in accord with accepted teaching. For instance, Muir and Ritchie (*Manual of Bacteriology*, 1937, London, p. 414) state that dried phthisical sputum has been found to contain virulent bacilli after two months. Another authority gives a life of ten days or more in road dust, or up to two months if kept in the dried state in the dark. The latter condition might well be found in an untreated library book. I may say that this question is of particular interest to me, since I have for some time been considering the problem of the provision of separate library facilities for tuberculous patients not in hospital.

Cause of Rib Fracture.—Dr. KEVIN BYRNE (Lakemba, New South Wales) writes: A patient—muscularly strong—owner of a dairy, used to collect as cow-feed waste cabbages from Sydney's "Paddy's Markets," tossing them on a large fork over a high-sided receptacle fitted to his lorry. One day a particularly heavy forkful slipped off as he started to toss. The anticipated exertion was used on the lightened load. Muscular effort alone accounted for six very badly fractured ribs, three on each side.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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